2ND Search

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L17

L18

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(FILE 'HOME' ENTERED AT 16:21:07 ON 18 NOV 2004)

FIGE VREGUSHRAY ENTERED AT 16:21:24 ON 18 NOV 2004
251 .CYWKVCT/SOSP yy il and c6-c6/es 162

FILE 'HCAPLUS' ENTERED AT 16:25:29 ON 18 NOV 2004 L3

FILE 'REGISTRY' ENTERED AT 16:25:41 ON 18 NOV 2004 SAVE TEMP L1 AUD087F0/A

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=> b hcap FILE 0HCAPLUS ENTERED AT 16:30:51 ON 18 NOV 2004 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2004 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 18 Nov 2004 VOL 141 ISS 21 FILE LAST UPDATED: 17 Nov 2004 (20041117/ED)

58 L16 AND P/DT

37 L17 AND US/PC

ILL LALV AND US/PC.B

This file contains CAS Registry Numbers for easy and accurate substance identification.

## as हा होता तत्त्व त्राहर

- ANSWER 1 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN L14
- AN 2003:875153 HCAPLUS
- 139:369779 DN
- ED Entered STN: 07 Nov 2003
- Multifaceted endovascular stent copolyester coating for preventing TI restenosis
- IN Shalaby, Shalaby W.
- PA
- Poly-Med, Inc., USA PCT Int. Appl., 18 pp. SO

Search done by Noble Jarrell

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CODEN: PIXXD2
DT
     Patent
     English
LA
IC
     ICM A61L031-10
         A61L031-16
     ICS
CC
     63-7 (Pharmaceuticals)
FAN.CNT 1
     PATENT NO.
                          KIND
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
     WO 2003090807
                                 20031106
                                              WO 2003-US12831
                                                                      20030423
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PRAI US 2002-375182P
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CLASS
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                 CLASS PATENT FAMILY CLASSIFICATION CODES
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 WO 2003090807
                 ICM
                         A61L031-10
                 ICS
                        A61L031-16
     This invention deals with a carboxyl-bearing, amphiphilic, solid
AB
     copolyester stent coating composition for multifaceted prevention of vascular
     restenosis through a plurality of physicopharmacol. modes. The composition
     includes one or more bioactive compds. and a copolymn. product of
     polyalkylene glycol, end-grafted with one or more cyclic monomer and
     treated further to introduce carboxyl-bearing end or side groups. The
     invention also deals with bioactive agents in an ionically conjugated
     form. The present coating may be applied to a metallic or an absorbable
     polymeric stent for use in preventing vascular restenosis. For example,
     an absorbable, amphiphilic copolyester with carboxy-bearing side group was
     prepared by polyethylene glycol end-grafting with .epsilon.-caprolactone and
     L-lactide by a ring-opening mechanism and maleation in the presence of free radical initiator. The copolyester was then ionically conjugated
     with lanreotide acetate and trapidil hydrochloride and lyophilized to
     yield solid conjugates.
ST
     polyester drug stent coating vascular restenosis
     Peptides, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (antiangiogenic; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
     Polyesters, biological studies
IT
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (block; multifaceted endovascular stent coating comprising bioactive
        compound and copolyester for preventing restenosis)
TТ
     Artery, disease
        (coronary, restenosis; multifaceted endovascular stent coating
        comprising bioactive compound and copolyester for preventing restenosis)
IT
     Angiogenesis inhibitors
     Antitumor agents
     Coating materials
     Platelet aggregation inhibitors
        (multifaceted endovascular stent coating comprising bioactive compound
        and copolyester for preventing restenosis)
TΤ
     Polyesters, biological studies
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (multifaceted endovascular stent coating comprising bioactive compound
        and copolyester for preventing restenosis)
TT
     Anti-inflammatory agents
        (nonsteroidal; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
IT
     Polyoxyalkylenes, biological studies
     RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (polyester-, block; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
IΤ
     Polyoxyalkylenes, biological studies
```

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RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (polyester-; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
IT
     Polyesters, biological studies
     RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (polyoxyalkylene-, block; multifaceted endovascular stent coating
        comprising bioactive compound and copolyester for preventing restenosis)
TT
     Polyesters, biological studies
     RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (polyoxyalkylene-; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
     Artery, disease
IT
        (restenosis; multifaceted endovascular stent coating comprising
        bioactive compound and copolyester for preventing restenosis)
TT
     Medical goods
        (stents; multifaceted endovascular stent coating comprising bioactive
        compound and copolyester for preventing restenosis)
IT
     188626-10-0DP, maleated
     RL: DEV (Device component use); SPN (Synthetic preparation); THU
     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (multifaceted endovascular stent coating comprising bioactive compound
        and copolyester for preventing restenosis)
IT
     9034-40-6D, LHRH, analogs 22204-53-1, Naproxen
                                                          26852-64-2, Trapidil
     hydrochloride 33069-62-4, Paclitaxel
                                               51110-01-1D, Somatostatin,
     analogs 127984-74-1, Lanreotide acetate
     RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological
     study); USES (Uses)
        (multifaceted endovascular stent coating comprising bioactive compound
        and copolyester for preventing restenosis)

11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 11
RE
(1) Angiotech Pharm Inc; WO 9921908 A 1999 HCAPLUS
(2) Ivan, B; US 5073381 A 1991 HCAPLUS
(3) Jarr, E; PROCEEDINGS OF THE INTERNATIONAL SYMPOSIUM ON CONTROLLED RELEASE
    BIOACTIVE MATERIALS 1999, V26, P631
(4) Kuzma, J; US 5993972 A 1999 HCAPLUS
(5) Poly Med Inc; EP 0737703 A 1996 HCAPLUS
(6) Poly Med Inc; EP 0952171 A 1999 HCAPLUS
(7) Scimed Life Systems Inc; WO 0101890 A 2001 HCAPLUS
(8) Seok, K; US 6210717 B1 2001 HCAPLUS
(9) Shalaby, S; US 2002164365 A1 2002
(10) Stanslaski, J; US 2001032014 A1 2001
(11) William, L; WO 02055122 A 2002 HCAPLUS
L14 ANSWER 2 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
NΑ
    2002:850147 HCAPLUS
DN
     137:358135
ED
     Entered STN: 08 Nov 2002
     Multifaceted compositions for post-surgical adhesion prevention
     Shalaby, Shalaby W.; Shalaby, Waleed S. W.; Shalaby, Marc
IN
PA
     U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S. 6,413,539.
SO
     CODEN: USXXCO
DT
     Patent
LA
     English
     ICM A61F002-00
TC
NCL
     424426000
     63-6 (Pharmaceuticals)
FAN.CNT 4
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                                 DATE
                                              APPLICATION NO.
                                                                      DATE
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     US 2002164365
                          A1
                                 20021107
                                              US 2002-131657
                                                                      20020424
     US 6551610
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                                 20030422
     US 6413539
                           B1
                                 20020702
                                              US 1998-16439
                                                                      19980129
PRAI US 1995-421222
                                 19950413
                           A3
     US 1996-740646
                           A2
                                 19961031
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19980129

CLASS PATENT FAMILY CLASSIFICATION CODES

A2

US 1998-16439

CLASS PATENT NO.

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 US 2002164365
                        A61F002-00
                 NCL
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                       A61K006/087; A61L031/04B; A61L031/06; A61L031/06;
                 ECLA
                        A61L031/14F; C08G063/4; C08G063/664; A61K009/00M4;
                        A61K047/34; A61K047/48K6; A61K047/48W8; A61L024/04R;
                       A61L; A61L026/00B4; A61L026/00H7
A61L031/06; C08G063/664
US 6413539
                 ECLA
    This invention deals with an absorbable, gel-forming composition for
     multifaceted prevention of post-operative surgical adhesion through a
     plurality of physico-pharmacol. modes, comprising a solution of one or more
     bioactive compds. in a liquid copolymeric vehicle made by end-grafting one
     or more cyclic monomer onto a polyalkylene glycol. More specifically, the
    bioactive drugs can display one or more pharmacol. activity associated with
     antiangiogenic, antineoplastic, anti-inflammatory, and anti-proliferative
     effects.
    post surgical adhesion prevention
     Polyoxyalkylenes, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (grafts; multifaceted compns. for post-surgical adhesion prevention)
     Adhesion, biological
     Antitumor agents
        (multifaceted compns. for post-surgical adhesion prevention)
     Polyoxyalkylenes, biological studies
IT
     Proteins
    RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (multifaceted compns. for post-surgical adhesion prevention)
IT
    Anti-inflammatory agents
        (nonsteroidal; multifaceted compns. for post-surgical adhesion
        prevention)
    Peptides, biological studies
TΤ
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (octapeptides, cyclic; multifaceted compns. for post-surgical adhesion
        prevention)
IT
     Polyethers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (polyester-, aliphatic; multifaceted compns. for post-surgical adhesion
        prevention)
ΙT
     Polyesters, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (polyether-, aliphatic; multifaceted compns. for post-surgical adhesion
        prevention)
     9034-40-6D, Lhrh, analogs 15421-84-8, Trapidil
                                                       22204-53-1, Naproxen
IT
     25322-68-3, Polyethylene glycol 33069-62-4, Paclitaxel 51110-01-1D,
     Somatostatin, analogs 108736-35-2, Lanreotide 113497-66-8
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (multifaceted compns. for post-surgical adhesion prevention)
L14 ANSWER 3 OF 34 HCAPLUS COPYRIGHT 2004 ACS, on STN
     2002:555963 HCAPLUS
AN
DN
     137:114538
     Entered STN: 26 Jul 2002
ED
     Ionic molecular conjugates of N-acylated derivatives of
ΤI
     poly(2-amino-2-deoxy-D-glucose) and polypeptides
ΤN
     Shalaby, Shalaby W.; Jackson, Steven A.;
     Ignatious, Francis X.; Moreau, Jacques-Pierre; Russell, Ruth
PA
     U.S. Pat. Appl. Publ., 14 pp., Cont.-in-part of U.S. Ser. No. 929,363.
SO
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DT
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LΑ
     English
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     ICM A61K009-00
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     63-6 (Pharmaceuticals)
     Section cross-reference(s): 34
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     EP 1123112
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                                                EP 1999-954780
                            A1
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                                    20010606
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                                                                            20010406
                                                  US 2002-251018
     -US 2003092800
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                             A1
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CLASS
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                          A61K038/31; A61K047/48K8; C08B037/00M3B2; C08L005/08
 US 2003092800
                  ECLA
    A copolymer comprising an N-acylated derivative, and a composition comprising said
     copolymer and a polypeptide, said polypeptide comprising at least one
     effective ionogenic amine, wherein at least 50 %, by weight, of said
     polypeptide present in said composition is ionically bound to said polymer.
     Conjugates were prepared from chitosan derivs. and a somatostatin
     polypeptide analog Somatuline.
     peptide acyl glucosamine polymer deriv conjugate; chitosan peptide
     conjugate drug delivery
IT
     Peptides, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (conjugates; oral pharmaceutical dosage forms for pulsatile delivery of
         an antiarrhythmic agent)
IT
     Drug delivery systems
         (oral pharmaceutical dosage forms for pulsatile delivery of an
         antiarrhythmic agent)
     9012-76-4, Chitosan 9012-76-4D, Chitosan, N-succinylated RL: RCT (Reactant); RACT (Reactant or reagent)
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
         glucose) and polypeptides)
     108-30-5DP, Succinic anhydride, reaction products with depolymd. chitosan
     108-55-4DP, Glutaric anhydride, reaction products with depolymd. chitosan
     123-62-6DP, Propionic anhydride, reaction products with depolymd. chitosan
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
         glucose) and polypeptides)
     9012-76-4DP, Chitosan, depolymd., acyl derivs., conjugates with peptides
     35110-26-0DP, acyl derivs., conjugates with peptides 53714-56-0DP,
     conjugates 57773-63-4DP, conjugates 57773-65-6DP, conjugates 57982-77-1DP, conjugates 64717-45-9DP, conjugates 65807-02-5I conjugates 66866-63-5DP, conjugates 76712-82-8DP, conjugates
                                                                  65807-02-5DP
     78115-75-0DP, conjugates 127984-74-1DP, Somatuline, conjugates
     with acyl chitosan derivs. 132609-33-7DP, conjugates
     148440-40-8DP, conjugates 204388-13-6DP, conjugates 204388-14-7DP, conjugates 215937-92-1DP, conjugates
                                                                    215945-52-1DP,
     conjugates
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
         glucose) and polypeptides)
     51110-01-1D, Somatostatin, analogs
     RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (oral pharmaceutical dosage forms for pulsatile delivery of an
         antiarrhythmic agent)
     9002-64-6. Parathyroid hormone
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (oral pharmaceutical dosage forms for pulsatile delivery of an
         antiarrhythmic agent)
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L14 ANSWER 4 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     2001:560059 HCAPLUS
     135:132468
DN
     Entered STN: 03 Aug 2001
ED
     Method of inhibiting fibrosis with a somatostatin or somatostatin agonist
ΤI
     Culler, Michael D.; Kasprzyk, Philip G.
IN
     Biomeasure Inc., USA
PA
     U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 705,790, abandoned.
SO
     CODEN: USXXAM
DT
     Patent
LΑ
     English
     ICM A61K038-00
     ICS C07K005-00; C07K007-00
NCL
     514012000
     1-12 (Pharmacology)
CC
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CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                 ICM
                        A61K038-00
                        C07K005-00; C07K007-00
                 ICS
                        514012000
                 NCL
os
    MARPAT 135:132468
AB
     The invention discloses a method of inhibiting fibrosis in a patient. The
     method comprises administering a therapeutically effective amount of a
     somatostatin, a somatostatin agonist, or a pharmaceutically acceptable
     salt thereof, to the patient.
     somatostatin agonist fibrosis inhibition
ST
     Human immunodeficiency virus
IT
     Kidney, disease
        (HIV nephropathy; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR1; somatostatin or somatostatin agonist for fibrosis inhibition)
IT
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR2; somatostatin or somatostatin agonist for fibrosis inhibition)
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR3; somatostatin or somatostatin agonist for fibrosis inhibition)
IT
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR4; somatostatin or somatostatin agonist for fibrosis inhibition)
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR5; somatostatin or somatostatin agonist for fibrosis inhibition)
IT
     Transplant rejection
        (allotransplant; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Nervous system
        (central, disease, fibrosis; somatostatin or somatostatin agonist for
        fibrosis inhibition)
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Audet 09/870087

Page 7

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IT
     Kidney, disease
        (diabetic nephropathy; somatostatin or somatostatin agonist for
        fibrosis inhibition)
IT
     Toxicity
        (drug, fibrosis; somatostatin or somatostatin agonist for fibrosis
        inhibition)
     Eosinophilia
IT
        (eosinophilia-myalgia syndrome; somatostatin or somatostatin agonist
        for fibrosis inhibition)
IT
     Environment
        (fibrosis induced by environmental factor; somatostatin or somatostatin
        agonist for fibrosis inhibition)
IT
    Immune system
        (fibrosis induced by immune reaction; somatostatin or somatostatin
        agonist for fibrosis inhibition)
IT
    Chemotherapy
    Disease, animal
     Drugs
     Radiation
     Wound
        (fibrosis induced by; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Bone, disease
     Cardiovascular system
     Digestive tract
     Endocrine system
     Kidney, disease
     Liver, disease
Lung, disease
     Skin, disease
        (fibrosis; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Drugs
        (gastrointestinal; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Kidney, disease
        (glomerulonephritis; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Environment
        (industrial, fibrosis induced by industrial factor; somatostatin or
        somatostatin agonist for fibrosis inhibition)
        (intraocular; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
     Myeloproliferative disorders
        (myelofibrosis; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
    Drug delivery systems
        (oral; somatostatin or somatostatin agonist for fibrosis inhibition)
IT
     Drug delivery systems
        (parenterals; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
        (scar; somatostatin or somatostatin agonist for fibrosis inhibition)
     Cardiovascular agents
     Cirrhosis
     Drug delivery systems
     Fibrosis
     Keloid
     Nervous system agents
        (somatostatin or somatostatin agonist for fibrosis inhibition)
IT
     Drug delivery systems
        (sustained-release; somatostatin or somatostatin agonist for fibrosis
        inhibition)
IT
     Skin, disease
        (systemic skin sclerosis; somatostatin or somatostatin agonist for
        fibrosis inhibition)
IT
    Drug delivery systems
        (topical; somatostatin or somatostatin agonist for fibrosis inhibition)
TT
    Liver, disease
        (veno-occlusive disease; somatostatin or somatostatin agonist for
        fibrosis inhibition)
IT
     Transforming growth factors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
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        (somatostatin or somatostatin agonist for fibrosis inhibition)
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RE
(1) Border; Nature 1992, V360, P361 HCAPLUS
(2) Border, W; Exp Nephrol 1994, V2, P13 HCAPLUS
(3) Border, W; The New England J of Med 1994, V331(19), P1286 HCAPLUS
(4) Coy; US 4904642 1990 HCAPLUS
(5) Lundergan, C; Atherosclerosis 1989, V80, P49 HCAPLUS
(6) Lyles, K; J Bone Miner Res 1997, V12(6), P929 MEDLINE
(7) Mizoi, T; Cancer Res 1993, V53(1), P183 HCAPLUS
(8) Najean, Y; Leuk Lymphoma 1996, V22(Suppl 1), P111
(9) Smiley, J; Am J Med Sci 1992, V304(5), P319 MEDLINE
(10) Tahara, E; J Cancer Res Clin Oncol 1990, V116(2), P121 MEDLINE
(11) Tracy; Am J Pathol 1993, V143(6), P1574 HCAPLUS
(12) Tracy, T; Am J Pathol 1993, V143(6), P1574 HCAPLUS
(13) Tsukamoto; Endocrine Journal 1994, V41(4), P437 MEDLINE (14) Tsukamoto; Endocrine Journal 1994, V41(4), P437 MEDLINE
(15) Wahl, S; Kidney International 1997, V51, P1370 HCAPLUS
L14 ANSWER 5 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     2001:297646 HCAPLUS
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DN
ED
     Entered STN: 26 Apr 2001
     Ionic molecular conjugates of biodegradable polyesters and bioactive
ΤI
     polypeptides
IN
     Shalaby, Shalaby Wahba; Jackson, Steven A.; Moreau,
     Jacques-Pierre
PA
     Societe de Conseils de Recherches et d'Applications Scientifiques (SCRAS),
     Fr.
SO
     U.S., 17 pp., Cont.-in-part of U.S. 5,863,985.
     CODEN: USXXAM
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     English
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                   ECLA
                          A61K047/48K6; C07K007/23; C07K014/655
 WO 9415587
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                          A61K047/48K6; C07K007/23; C07K014/655
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                          C07K014/655
AB
    Disclosed is a sustained release pharmaceutical composition The composition
     includes a polyester containing a free COOH group ionically conjugated with a
     bioactive polypeptide comprising at least one effective ionogenic amine,
     wherein at least 50% by weight of the polypeptide present in the composition is ionically conjugated to the polyester. The polyesters contain citric acid
     or tartaric acid.
     biodegradable polyester polypeptide ionic mol conjugate; sustained release
     pharmaceutical
TT
     Polyesters, preparation
     RL: IMF (Industrial manufacture); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation);
         (conjugates with bioactive polypeptides; ionic mol. conjugates of
         biodegradable polyesters and bioactive polypeptides)
IT
     Enkephalins
     Peptides, preparation
     Tachvkinins
     RL: IMF (Industrial manufacture); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation);
         (conjugates with polyesters; ionic mol. conjugates of biodegradable
         polyesters and bioactive polypeptides)
TT
     Drug delivery systems
         (sustained-release; ionic mol. conjugates of biodegradable polyesters
         and bioactive polypeptides)
IT
     105953-91-1P, Neuromedin
     RL: IMF (Industrial manufacture); TEM (Technical or engineered material
     use); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation);
     USES (Uses)
         (conjugates with polyesters; ionic mol. conjugates of biodegradable
         polyesters and bioactive polypeptides)
IT
     58-82-2DP, Bradykinin, conjugates with polyesters 1393-25-5DP, Secretin,
     conjugates with polyesters 9002-60-2DP, ACTH, conjugates with polyesters
     9002-64-6DP, PTH, conjugates with polyesters 9002-71-5DP, TSH, conjugates with polyesters 9002-79-3DP, MSH, conjugates with polyesters
     conjugates with polyesters
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9007-12-9DP, Calcitonin, conjugates with polyesters
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     Glucagon, conjugates with polyesters, preparation 9034-40-6DP, LHRH,
     conjugates with polyesters 33507-63-0DP, Substance P, conjugates with polyesters 37221-79-7DP, VIP, conjugates with polyesters 39379-15-2DP, Neurotensin, conjugates with polyesters 51110-01-1DP, Somatostatin,
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     106602-62-4DP, Amylin, conjugates with polyesters 108736-35-2DP,
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         (ionic mol. conjugates of biodegradable polyesters and bioactive
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               THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; EP 0107591 A2 1984 HCAPLUS
(2) Anon; EP 0426055 A3 1991 HCAPLUS
(3) Anon; EP 0467389 A2 1992
(4) Anon; EP 0483429 Al 1992 HCAPLUS
(5) Anon; WO 9211844 1992 HCAPLUS
(6) Anon; WO 9317668 1993 HCAPLUS
(7) Anon; WO 9415587 1994 HCAPLUS
(8) Boswell; US 3773919 1973 HCAPLUS
(9) Dean; US 5162505 1992 HCAPLUS
(10) Hess; US 5084553 1992 HCAPLUS
(11) Hutchinson; US 4767628 1988 HCAPLUS
(12) Mehta, R; J of Controlled Release 1994, V29, P375 HCAPLUS
(13) Nowinski; US 4609707 1986 HCAPLUS
(14) Pappin; US 5071909 1991 HCAPLUS
(15) Peterson; US 4356166 1982 HCAPLUS
(16) Ruiz; US 5569467 1996 HCAPLUS
(17) Shah; J of Controlled Realeas 1992, V18, P261 HCAPLUS
(18) Shalaby; US 5672659 1997 HCAPLUS
(19) Shalaby; US 5863985 1999 HCAPLUS
L14 ANSWER 6 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
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     Preparation of ionic molecular conjugates of biodegradable polyesters and
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IN
     Shalaby, Shalaby W.; Jackson, Steven A.; Moreau,
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PA
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     PCT Int. Appl., 46 pp.
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     63-6 (Pharmaceuticals)
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 US 6221958
                 ECLA
   A sustained-release pharmaceutical composition includes a polyester containing a
     free COOH group ionically conjugated with a bioactive peptide comprising
     at least 1 effective ionogenic amine, wherein at least 50% by weight of the
     peptide present in the composition is ionically conjugated to the polyester.
     Thus, a rod delivery system was obtained by synthesizing the citric acid ester of .epsilon.-caprolactone-glycolide copolymer followed by treatment
     with the peptide, LHRH acetate. The ionic conjugate and the polymer were
     melted and the melted materials was extruded into rods.
ST
     ionic conjugate polyester bioactive peptide prepn
     Peptides, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (conjugates; preparation of ionic mol. conjugates of biodegradable
        polyesters and bioactive peptides)
TΤ
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IT
     Peptides, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (growth hormone releasing; preparation of ionic mol. conjugates of
        biodegradable polyesters and bioactive peptides)
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     Polyesters, biological studies
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(hydroxycarboxylic acid-based; preparation of ionic mol. conjugates of
        biodegradable polyesters and bioactive peptides)
IT
     Drug delivery systems
        (implants, rods; preparation of ionic mol. conjugates of biodegradable
        polyesters and bioactive peptides)
IT
     Polyesters, biological studies
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
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        (polycarbonate-; preparation of ionic mol. conjugates of biodegradable
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     Polycarbonates, biological studies
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        polyesters and bioactive peptides)
IΤ
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of ionic mol. conjugates of biodegradable polyesters and
        bioactive peptides)
IT
     Enkephalins
     Tachykinins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of ionic mol. conjugates of biodegradable polyesters and
        bioactive peptides)
IT
     Drug delivery systems
        (sustained-release; preparation of ionic mol. conjugates of biodegradable
        polyesters and bioactive peptides)
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34346-01-5P, Glycolic acid-lactic

9034-40-6DP, LHRH, polymer conjugates

acid copolymer 286411-58-3P, Glycolic acid-L-lactide-malic acid

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copolymer salt with D-Trp6[LHRH] 286411-59-4P,
     Glycolide-L-lactide-malic acid copolymer salt with BIM 23014
     286427-72-3P, Glycolic acid-L-lactide copolymer ester with malic acid
     286427-74-5P, Glycolide-L-lactide copolymer ester with malic acid
     286427-75-6P, Glycolide-DL-lactide copolymer ester with citric acid
     286427-77-8P, Glycolide-DL-lactide copolymer ester with 1,6-hexanediol
     286427-80-3P, Glycolic acid-L-lactic acid-malic acid copolymer salt with
     D-Trp6 [LHRH] 286427-81-4P, Glycolic acid-L-lactic acid-malic
     acid copolymer salt with BIM 23014
                                           286427-84-7P, .epsilon.-Caprolactone-
     Glycolide copolymer ester with citric acid salt with LHRH acetate
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     (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
     (Uses)
        (preparation of ionic mol. conjugates of biodegradable polyesters and
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     USES (Uses)
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        bioactive peptides)
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     ester with tartaric acid salt with LHRH acetate 286427-88-1P,
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     with LHRH acetate
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     study); PREP (Preparation); USES (Uses)
        (preparation of ionic mol. conjugates of biodegradable polyesters and
        bioactive peptides)
               Bradykinin 1393-25-5, Secretin 9002-60-2, ACTH, biological 9002-64-6, PTH 9002-71-5, TSH 9002-79-3, MSH 9007-12-9,
     58-82-2, Bradykinin 1393-25-5, Secretin
     studies
     Calcitonin 9007-92-5, Glucagon, biological studies
                                                               9034-39-3, Growth
                                                           37221-79-7, VIP
     hormone releasing factor 33507-63-0, Substance P
     39379-15-2, Neurotensin
                                51110-01-1, Somatostatin
                                                            52906-92-0, Motilin
     80043-53-4, Gastrin-releasing peptide 82785-45-3, Neuropeptide Y
     83652-28-2, CGRP 103370-86-1, PTH-related protein 105953-91-1,
                 106388-42-5, Peptide YY 106602-62-4, Amylin 119418-04-1,
     Neuromedin
              137061-48-4, PACAP 286411-57-2
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (preparation of ionic mol. conjugates of biodegradable polyesters and
        bioactive peptides)
RE.CNT
              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD

    Touraud Franck Jean Claude; WO 9739738 A 1997 HCAPLUS
    Touraud Frank Jean Claude; WO 9740085 A 1997 HCAPLUS

L14 ANSWER 7 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     2000:314581 HCAPLUS
     132:339360
     Entered STN: 15 May 2000
     Lactone-bearing absorbable polymers for drug sustained release
     Ignatious, Francis X.
     Biomeasure Incorporated, USA
     PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
     Patent
     English
     ICM A61K047-48
     ICS C08G064-00; C08G067-04; C08G079-02; C08G063-08
     63-6 (Pharmaceuticals)
     Section cross-reference(s): 37
FAN.CNT 1
     PATENT NO.
                                 DATE
                                              APPLICATION NO.
                                                                      DATE
                          KIND
                                 20000511
                                              WO 1999-US25706
                                                                      19991102
     WO 2000025826
                           A1
         W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
             CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
             IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
             MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI,
             SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
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CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                            CA 1999-2349346
     CA 2349346
                          AA
                                20000511
                                                                    19991102
     EP 1144013
                                            EP 1999-958738
                                                                    19991102
                          A1
                                20011017
         R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
             IE, SI, LT, LV, FI, RO
     JP 2002528602
                          T2
                                20020903
                                            JP 2000-579264
                                                                    20010502
                                20010629
                                            NO 2001-2161
     NO 2001002161
                          Α
PRAI US 1998-106708P
                          P
                                19981102
     US 1998-184413
                          A1
                                19981102
     WO 1999-US25706
                          W
                                19991102
CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
WO 2000025826
                 ICM
                        A61K047-48
                        C08G064-00; C08G067-04; C08G079-02; C08G063-08
                 TCS
WO 2000025826
                 ECLA
                        C08G063/08; C08G064/00; C08G067/04
    The present invention pertains to biodegradable polymers comprising a
     non-polymerizable lactone, biodegradable compns. comprising the polymer
     and a therapeutic agent, the use of the compns. for the sustained release
     of therapeutic agents, wherein the therapeutic agent is reversibly
     immobilized on the polymer matrix using ionic complexation between the
     latent carboxylic groups present on the lactone bearing polymer matrix and
     a cationic group on the therapeutic agent. A polymer was obtained by
     reacting isocitric acid lactone with propanediol followed by treatment
     with dl-lactide and glycolide in the presence of stannous octoate.
     Lanreotide was immobilized on this polymer for later release from the
     drug.
ST
     sustained release drug polymer lactone prepn
     Polymers, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (biodegradable; preparation of lactone-bearing absorbable polymers for drug
        sustained release)
IT
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (dilactone-based; preparation of lactone-bearing absorbable polymers for
        drug sustained release)
IT
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (lactide; preparation of lactone-bearing absorbable polymers for drug sustained release)
IT
     Drug delivery systems
        (microparticles, sustained-release; preparation of lactone-bearing
        absorbable polymers for drug sustained release)
TΤ
     Drug delivery systems
        (microspheres, sustained-release; preparation of lactone-bearing absorbable
        polymers for drug sustained release)
IT
     Polyethers, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (ortho ester group-containing; preparation of lactone-bearing absorbable
        polymers for drug sustained release)
TТ
     Tachykinins
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
     use); BIOL (Biological study); PROC (Process); USES (Uses)
        (preparation of lactone-bearing absorbable polymers for drug sustained
        release)
IT
     Polyanhydrides
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of lactone-bearing absorbable polymers for drug sustained
        release)
IT
     Polycarbonates, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of lactone-bearing absorbable polymers for drug sustained
        release)
IT
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of lactone-bearing absorbable polymers for drug sustained
        release)
IT
     Polyphosphazenes
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
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study); PREP (Preparation); USES (Uses) (preparation of lactone-bearing absorbable polymers for drug sustained release) Lactones IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (preparation of lactone-bearing absorbable polymers for drug sustained release) TΤ Drug delivery systems (sustained-release; preparation of lactone-bearing absorbable polymers for drug sustained release) 58-82-2, Bradykinin 1393-25-5, Secretin 9002-60-2, ACTH, biological IT studies 9002-64-6, PTH 9002-71-5, TSH 9002-79-3, MSH 9007-12-9 Calcitonin 9007-92-5, Glucagon, biological studies 9034-40-6, LHRH 31362-50-2, Bombesin 39379-15-2, Neurotensin 51110-01-1, Somatostatin 57773-63-4 80043-53-4, Gastrin-releasing peptide 83652-28-2, CGRP 103370-86-1, Humoral hypercalcemic factor 105953-91-1, Neuromedin 105953-91-1, Neuromedin 106388-42-5, Peptide YY 106602-62-4, Amylin 108736-35-2 119418-04-1, Galanin 182153-96-4 234752-56-8 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (preparation of lactone-bearing absorbable polymers for drug sustained release) 26023-30-3DP, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)], ester with isopropylidene lactone 267893-40-3P 267893-41-4P 267893-42-5P IT 267893-43-6P RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (preparation of lactone-bearing absorbable polymers for drug sustained release) THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 1 RE (1) Kansai Paint Co Ltd; EP 0400108 A 1991 L14 ANSWER 8 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN 2000:260068 HCAPLUS AN DN 132:284253 ED Entered STN: 21 Apr 2000 Ionic molecular conjugates of N-acylated derivatives of poly(2-amino-2-deoxy-D-glucose) and polypeptides IN Shalaby, Shalaby W.; Jackson, Steven A.; Ignatious, Francis X.; Moreau, Jacques-Pierre; Russell, Ruth M. PΑ Societe De Conseils De Recherches Et D'applications Scientifiques S.A., Fr. so PCT Int. Appl., 34 pp. CODEN: PIXXD2 DT Patent LA English TC ICM A61K047-36 ICS A61K038-00; C08L005-08; C08B037-08 CC 63-6 (Pharmaceuticals) Section cross-reference(s): 2, 33, 34 FAN.CNT 3 PATENT NO. KIND DATE APPLICATION NO. DATE . PΙ WO 2000021567 20000420 WO 1999-US23406 19991008 A1 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG US 2002098206 A1 20020725 US 1998-169423 19981009 US 6479457 B2 20021112 CA 2346066 AA 20000420 CA 1999-2346066 19991008 EP 1999-954780 20010816 EP 1123112 A1 19991008 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO JP 2002527533 20020827 JP 2000-575539 19991008 T2 20010606 NO 2001-1744 20010406 NO 2001001744 Α PRAI US 1998-169423 A1 19981009 US 1995-468947 **A3** 19950606

US 1997-929363

A2

19970909

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WO 1999-US23406
                                  19991008
                            W
CLASS
                  CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
                          A61K047-36
 WO 2000021567
                  ICM
                  ICS
                          A61K038-00; C08L005-08; C08B037-08
 US 2002098206
                  ECLA
                          A61K038/31; C08B037/00M3B2
    A copolymer comprises an N-acylated derivative, and a composition comprising said
     copolymer and a polypeptide, said polypeptide comprising at least one
     effective ionogenic amine, wherein at least 50 percent, by weight, of said
     polypeptide present in said composition is ionically bound to said polymer.
     Chitosan was depolymd., succinylated, , acetylated, and conjugated to the
     somatostatin peptide analog Somatuline.
ST
     aminodeoxyglucose polymer peptide conjugate
IT
     Drug delivery systems
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
        glucose) and polypeptides)
IT
     127984-74-1DP, Somatuline, conjugates with poly(N-acyl-D-
     glucosamine) s
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
        glucose) and polypeptides)
TT
     108-30-5D, Succinic anhydride, reaction products with depolymd.chitosan,
     conjugates with peptides
                                  108-55-4D, Glutaric anhydride, reaction
     products with depolymd.chitosan, conjugates with peptides
                                                                     123-62-6D
     Propionic anhydride, reaction products with depolymd.chitosan, conjugates
     with peptides 9012-76-4D, Chitosan, depolymd., acyl derivs., conjugates with peptides 35110-26-0D, D-Glucose, 2-amino-2-deoxy-, homopolymer, N-acyl derivs., conjugates with peptides 38234-21-8D, Fertirelin,
     conjugates with poly (N-acyl-D-glucosamine) s 53714-56-0D, Leuprorelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       57773-63-4D, Tryptorelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       57773-65-6D, Deslorelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       57982-77-1D, Buserelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       65807-02-5D, Goserelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       66866-63-5D, Lutrelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                       76712-82-8D, Histrelin,
     conjugates with poly(N-acyl-D-glucosamine)s
                                                      76932-56-4D, Nafarelin,
     conjugates with poly (N-acyl-D-glucosamine) s 113294-82-9D,
     conjugates with poly(N-acyl-D-glucosamine)s 204388-13-6D, conjugates
                                           215937-92-1D, conjugates with
     with poly(N-acyl-D-glucosamine)s
     poly (N-acyl-D-glucosamine) s
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (ionic mol. conjugates of N-acylated derivs. of poly(2-amino-2-deoxy-D-
        glucose) and polypeptides)
               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT
RE
(1) Biomeasure Inc; WO 9504752 A 1995 HCAPLUS
(2) Kent, J; US 4675189 A 1987 HCAPLUS
(3) McNeil Ppc Inc; EP 0643963 A 1995 HCAPLUS
(4) Shalaby, S; WO 9639160 A 1996 HCAPLUS
(5) Song, Y; JOURNAL OF CONTROLLED RELEASE V42(1), P93
     ANSWER 9 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
L14
     2000:133567 HCAPLUS
AN
DN
     132:185418
     Entered STN: 25 Feb 2000
ED
     Phosphorylated polymers and conjugates thereof
TΤ
IN
     Shalaby, Shalaby Wahba; Corbett, Joel Thomas
     Poly-Med, Inc., USA
PCT Int. Appl., 26 pp.
PA
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM A61K047-48
63-5 (Pharmaceuticals)
IC
CC
     Section cross-reference(s): 34, 35
FAN.CNT 1
     PATENT NO.
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                                   DATE
                                                APPLICATION NO.
                                                                         DATE
PΙ
     WO 2000009166
                                   20000224
                                                WO 1999-US18146
                                                                         19990810
                            A2
     WO 2000009166
                            Α3
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          W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
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              IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
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SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
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                                                                       19990810
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                                               AU 1999-54755
                                                                       19990810
                                              EP 1999-941024
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            AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
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     JP 2002522596
                           T2
                                  20020723
                                               JP 2000-564667
                                               RU 2001-106640
                           C2
                                  20030420
                                                                       19990810
     RU 2202563
     NO 2001000682
                           Α
                                  20010327
                                              NO 2001-682
                                                                       20010209
PRAI US 1998-131472
                           A1
                                  19980810
     US 1998-95875P
                           Ρ
                                  19980810
     WO 1999-US18146
                           W
                                  19990810
CLASS
                  CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
 WO 2000009166 ICM
                         A61K047-48
    The present invention is directed to absorbable polyesters comprising one
     or more monophosphate functionality; a conjugate comprising the foregoing
     polyester and a peptide and/or a bioactive agent; microparticles
     comprising an absorbable polyester; a conjugate comprising the
     microparticles and a peptide and/or a bioactive agent; an acylated or
     alkylated polysaccharide having one or more monophosphate functionality; a
     conjugate comprising the acylated or alkylated polysaccharide and a
     peptide and/or a bioactive agent and pharmaceutical compns. thereof. A
     polyester was prepared from caprolactone and diethylene glycol,
     phosphorylated and conjugated to a LHRH analog p-Glu-His-Trp-Ser-Tyr-D-Trp-
     Leu-Arg-Pro-Gly-NH2.
     polyester phosphate peptide conjugate absorbable
ST
TT
     Adhesives
     Adhesives
        (biol. tissue; absorbable phosphorylated polyester-peptide conjugates
        for pharmaceuticals)
TΤ
     Peptides, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (conjugates, with phosphorylated polyesters; absorbable phosphorylated
        polyester-peptide conjugates for pharmaceuticals)
IT
     Drug delivery systems
        (controlled-release; absorbable phosphorylated polyester-peptide
        conjugates for pharmaceuticals)
IT
     Polyesters, biological studies
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
         (phosphorylated, conjugates with peptides; absorbable phosphorylated
        polyester-peptide conjugates for pharmaceuticals)
IT
     Medical goods
        (tissue adhesives; absorbable phosphorylated polyester-peptide
        conjugates for pharmaceuticals)
TТ
     2466-09-3DP, Diphosphoric acid, reaction products with polyesters,
     conjugates with peptides 17465-86-0DP, gamma.-Cyclodextrin, phosphorylated, conjugates with peptides 26202-08-4DP, ester
                                                   26202-08-4DP, ester
     26780-50-7DP, phosphorylated, conjugates with peptides
                                                                 30846-39-0DP,
                                                  52305-30-3DP, phosphorylated,
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     conjugates with peptides 57773-63-4DP, conjugates with phosphorylated
                 75035-33-5DP, phosphorylated, conjugates with peptides
     108736-35-2DP, conjugates with phosphorylated polyesters 182153-96-4DP, conjugates with phosphorylated polyesters
                                                                    234752-56-8DP.
                                                   261921-43-1DP, phosphorylated,
     conjugates with phosphorylated polyesters
     conjugates with peptides
                                 287197-62-0DP, phosphorylated, conjugates with
     peptides
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
        (absorbable phosphorylated polyester-peptide conjugates for
        pharmaceuticals)
L14 ANSWER 10 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     2000:98356 HCAPLUS
     132:132776
DN '
ED
     Entered STN: 11 Feb 2000
ΤI
     Methods of using a somatostatin analogue in therapy
IN
     Moreau, Jacques-Pierre
     Biomeasure Incorporated, USA
PA
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PCT Int. Appl., 11 pp.
     CODEN: PIXXD2
DТ
     Patent
LΑ
     English
     ICM A61K038-00
IC
     2-5 (Mammalian Hormones)
CC
FAN. CNT 1
     PATENT NO.
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                               DATE
                                             APPLICATION NO.
                                                                     DATE
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     WO 2000006185
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                                             WO 1999-US17294
                                                                     19990729
                                 20000803
     WO 2000006185
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             MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM,
             TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD,
             RU, TJ, TM
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             CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
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                                 20020716
                                             JP 2000-562039
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                                             NZ 1999-509348
     NO 2001000481
                                             NO 2001-481
                          Α
                                 20010321
                                                                     20010129
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     ZA 2001000793
                          Α
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     EP 1291022
                          A1
                                20030312
                                             EP 2002-78746
                                                                     20020905
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             IE, SI, LT, LV, FI, RO, MK, CY, AL
PRAI US 1998-126525
                          A1
                                19980730
     US 1998-94693P
                          P
                                 19980730
     EP 1999-937658
                                 19990729
                          A3
     WO 1999-US17294
                          W
                                 19990729
CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 WO 2000006185 ICM
                        A61K038-00
                 ECLA
                        A61K038/12; A61K038/31
EP 1291022
   A method of treating one or more diseases and/or conditions using the
     somatostatin analog, H-.beta.-D-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2
     (where the cysteines are bonded by a disulfide bond) or a pharmaceutically
     acceptable salt thereof, most preferably the acetate salt of the compound
     Diseases and conditions such as gastroenterol. conditions and/or diseases,
     endocrinol. diseases and/or conditions, various types of cancers and
     conditions associated with cancer such as cancer cachexia, hypotension and
     panic attacks can be treated.
ST
     somatostatin analog therapeutic use
IT
     Bone, disease
        (Paget's; methods of using a somatostatin analog in treatment of
        various diseases or disorders)
IT
     Pancreas, neoplasm
        (VIPoma; methods of using a somatostatin analog in treatment of various
        diseases or disorders)
IT
     Pancreas, neoplasm
        (Zollinger-Ellison syndrome; methods of using a somatostatin analog in
        treatment of various diseases or disorders)
IT
     Pituitary gland
        (adenoma, gonadotropinoma; methods of using a somatostatin analog in
        treatment of various diseases or disorders)
IΤ
     Cachexia
        (cancerous; methods of using a somatostatin analog in treatment of
        various diseases or disorders)
IT
     Nerve, disease
        (diabetic neuropathy; methods of using a somatostatin analog in
        treatment of various diseases or disorders)
IT
        (disease, duodenogastric reflux; methods of using a somatostatin analog
        in treatment of various diseases or disorders)
TΤ
     Neoplasm
        (gastrinoma; methods of using a somatostatin analog in treatment of
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Page 18

Audet 09/870087 various diseases or disorders) IT Digestive tract (hemorrhage; methods of using a somatostatin analog in treatment of various diseases or disorders) Neoplasm IT (hypercalcemia of; methods of using a somatostatin analog in treatment of various diseases or disorders) Diarrhea TΤ (hypersecretory; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Intestine, disease (irritable bowel syndrome; methods of using a somatostatin analog in treatment of various diseases or disorders) Eye, disease IT (macula, degeneration; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Meninges (meningioma; methods of using a somatostatin analog in treatment of various diseases or disorders) Antidiarrheals IT Antihypertensives Antihypotensives Antitumor agents Anxiolytics Cushing's syndrome Hyperparathyroidism Psoriasis (methods of using a somatostatin analog in treatment of various diseases or disorders) Pancreas, disease IT (nesidoblastosis; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Intestine, disease (obstruction; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Anxiety (panic disorder; methods of using a somatostatin analog in treatment of various diseases or disorders) Hypertension (portal, complications of; methods of using a somatostatin analog in treatment of various diseases or disorders) TT Cirrhosis (postprandial portal venous hypertension in cirrhosis; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Hypertension (postprandial portal venous; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Pancreas, disease (pseudocysts and ascites; methods of using a somatostatin analog in treatment of various diseases or disorders) IT Connective tissue (scleroderma; methods of using a somatostatin analog in treatment of various diseases or disorders) 7440-70-2, Calcium, biological studies TT RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process) (hypercalcemia, of malignancy; methods of using a somatostatin analog in treatment of various diseases or disorders) 9004-10-8, Insulin, biological studies RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process) (hyperinsulinemia; methods of using a somatostatin analog in treatment

108736-35-2, Lanreotide 108736-35-2D, Lanreotide, salts 127984-74-1, Lanreotide acetate

of various diseases or disorders)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(methods of using a somatostatin analog in treatment of various diseases or disorders)

L14 ANSWER 11 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:670109 HCAPLUS

131:295567 DN

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ED
    Entered STN: 21 Oct 1999
     Inhibition of Helicobacter pylori proliferation
TI
    Kaneko, Hiroshi; Mitsuma, Terunori; Yamashita, Koichi; Morgan, Barry
IN
    Biomeasure, Inc., USA
PA
    U.S., 19 pp.
SO
    CODEN: USXXAM
DT
     Patent
     English
LA
     ICM A61K037-43
     ICS C07K007-26
    514009000
NCL
    1-5 (Pharmacology)
CC
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                                                                    DATE
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                                                                    19980507
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    WO 1999-US10058
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                        A61K037-43
                        C07K007-26
                 ICS
                        514009000
                 NCL
    MARPAT 131:295567
OS
AB
    The present invention is directed to a method of using somatostatin or a
     somatostatin agonist to inhibit the proliferation of Helicobacter pylori
     (H. pylori), which comprises administering to a patient in need thereof an
     effective amount of said somatostatin or somatostatin agonist. Preferably,
     a somatostatin sub-type receptor 2 (SSTR-2) selective somatostatin agonist
     is administered in a method of this invention. The inhibition of H.
     pylori proliferation is useful in treating various gastroduodenal diseases
     such as peptic ulcers, gastric cancer and gastric lymphoma.
    Helicobacter inhibitor somatostatin agonist; gastroduodenal disease
ST
     Helicobacter inhibitor somatostatin agonist
     Somatostatin receptors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (agonists; inhibition of Helicobacter pylori proliferation with
        somatostatin or a somatostatin agonist)
IT
    Digestive tract
        (disease; inhibition of Helicobacter pylori proliferation with
        somatostatin or a somatostatin agonist)
IT
    Lymphoma
        (gastric; inhibition of Helicobacter pylori proliferation with
        somatostatin or a somatostatin agonist)
IT
    Antibacterial agents
     Antitumor agents
     Antiulcer agents
     Helicobacter pylori
     Stomach, neoplasm
        (inhibition of Helicobacter pylori proliferation with somatostatin or a
        somatostatin agonist)
IT
    Ulcer
        (peptic; inhibition of Helicobacter pylori proliferation with
        somatostatin or a somatostatin agonist)
IT
     51110-01-1, Somatostatin
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
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(Uses) (agonists; inhibition of Helicobacter pylori proliferation with somatostatin or a somatostatin agonist) 72127-57-2 72127-59-4 72127-61-8 72127-62-9 76080-70-1 77236-35-2 77236-39-6 77236-42-1 77236-46-5 77286-22-7 79775-25-0 79775-28-3 79814-97-4 85003-75-4 85466-72-4 87778-83-4 87781-70-2 85466-73-5 85466-74-6 85549-65-1 95244-38-5 95310-74-0 95833-38-8 98044-71-4 90836-21-8 99660-13-6 103140-93-8 103222-03-3 103548-90-9 109605-17-6 109605-24-5 109605-27-8 109791-07-3 109791-08-4 109605-19-8 109985-46-8 110786-64-6 111857-96-6 113294-82-9 113294-83-0 113294-84-1 113294-89-6 120796-12-5 120796-15-8 144776-53-4 145758-77-6 150155-56-9 150957-55-4 152045-43-7 152045-44-8 152045-49-3 152045-40-4 152045-41-5 204387-62-2 204387-63-3 152510-40-2 173484-74-7 189192-34-5 204387-65-5 204387-66-6 204387-67-7 204387-68-8 204387-64-4 204387-71-3 204387-72-4 204387-73-5 204387-69-9 204387-70-2 204387-77-9 204387-78-0 204387-75-7 204387-76-8 204387-74-6 204387-81-5 204387-82-6 204387-79-1 204387-80-4 204387-83-7 204387-84-8 204387-85-9 204387-86-0 204387-87-1 204387-88-2 204387-91-7 204387-96-2 204387-97-3 204387-89-3 204387-90-6 204388-02-3 204388-03-4 204388-05-6 204388-06-7 204388-10-3 204388-14-7 204518-70-7 204518-71-8 204388-11-4 204388-13-6 205652-45-5 215937-92-1 215945-52-1 216259-64-2 216259-65-3 247032-69-5 247032-71-9 247032-72-0 216259-66-4 247032-68-4 247032-74-2 247032-75-3 247032-76-4 247032-77-5 247032-78-6 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (inhibition of Helicobacter pylori proliferation with somatostatin or a somatostatin agonist) THERE ARE 61 CITED REFERENCES AVAILABLE FOR THIS RECORD RE.CNT 61 (1) Alfven, G; Acta Paediatr 1993, V82, P967 MEDLINE (2) Anon; EP 0030920 B1 1981 HCAPLUS (3) Anon; GB 2095261 1982 HCAPLUS (4) Anon; FR 2522655 1982 HCAPLUS (5) Anon; WO 88027576 1988 (6) Anon; EP 0329295 Al 1989 HCAPLUS (7) Anon; EP 0363589 A2 1990 HCAPLUS (8) Anon; EP 0389180 B1 1990 HCAPLUS (9) Anon; EP 0395417 B1 1990 HCAPLUS (10) Anon; WO 9012811 1990 HCAPLUS (11) Anon; WO 9118016 1991 HCAPLUS (12) Anon; EP 0505680 B1 1992 HCAPLUS (13) Anon; WO 9701579 1997 HCAPLUS (14) Bauer; US 4395403 1983 HCAPLUS (15) Bauer; US 4435385 1984 HCAPLUS (16) Bauer; US 4728638 1988 HCAPLUS (17) Calam, J; Annals of Medicine 1995, V27, P569 HCAPLUS (18) Chiba, T; Gut Peptides: Biochemistry and Physiology 1994, P123 HCAPLUS (19) Coy; US 4485101 1984 HCAPLUS (20) Coy; US 4853371 1989 HCAPLUS (21) Coy; US 4871717 1989 HCAPLUS (22) Coy; US 4904642 1990 HCAPLUS (23) Freidinger; US 4235886 1980 HCAPLUS (24) Freidinger; US 4310518 1982 HCAPLUS (25) Freidinger; US 4360516 1982 HCAPLUS (26) Freidinger; US 4486415 1984 HCAPLUS (27) Gotz, J; Scand J Gastroenterol 1995, V30, P1064 MEDLINE (28) Haruma, K; Scand J Gastroenterol 1995, V30, P550 MEDLINE (29) Horvath, A; Peptides 1992, P533 (30) Hruby; US 4684620 1987 HCAPLUS (31) Kamber; US 4316890 1982 HCAPLUS (32) Kamber; US 4603120 1986 HCAPLUS (33) Kaneko, H; Digestive Diseases and Sciences 1992, V37(3), P409 MEDLINE (34) Kim; US 5552520 1996 HCAPLUS (35) Lee, J; Gastroenterology 1997, V113, PS99 MEDLINE (36) Marshall, B; The Lancet Jun 1984, Pl311 MEDLINE (37) Meyers; US 4224199 1980 HCAPLUS (38) Morgan; US 4585755 1986 HCAPLUS (39) Moss, S; The Lancet 1992, V340, P930 MEDLINE (40) Nutt; US 4522813 1985 HCAPLUS (41) Rao, R; Life Sciences 1991, V48(18), P1685 HCAPLUS (42) Rink; US 4238481 1980 HCAPLUS

(43) Rink; US 4328214 1982 HCAPLUS

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(44) Rink; US 4369179 1983 HCAPLUS
(45) Rivier; US 4211693 1980 HCAPLUS
(46) Sakakibara; US 4261885 1981 HCAPLUS
(47) Sandrin; US 4291022 1981 HCAPLUS
(48) Sarantakis; US 4190575 1980 HCAPLUS
(49) Sarantakis; US 4209426 1980 HCAPLUS
(50) Sarantakis; US 4215039 1980 HCAPLUS
(51) Sarantakis; US 4282143 1981 HCAPLUS
(52) Schally; US 4650787 1987 HCAPLUS
(53) Schally; US 4725577 1988 HCAPLUS
(54) Sieber; US 4358439 1982 HCAPLUS
(55) Sumii, M; Am J Gastroentero 1994, V89(9), P1515 MEDLINE
(56) Vale; US 4133782 1979 HCAPLUS
(57) van Binst, G; Peptide Research P8
(58) Veber; US 4146612 1979 HCAPLUS
(59) Veber; US 4190648 1980 HCAPLUS
(60) Villadsen; US 4224190 1980 HCAPLUS
(61) Warren, J; The Lancet 1983, P1273
L14 ANSWER 12 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1999:495196 HCAPLUS
AN
DN
     131:134661
ED
     Entered STN: 10 Aug 1999
TI
     Absorbable microparticles
     Shalaby, Shalaby Wahba
     Poly-Med Inc., USA
PA
     PCT Int. Appl., 54 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LΑ
     English
     ICM A61K047-48
63-6 (Pharmaceuticals)
IC
CC
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PRAI US 1998-15394
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     WO 1999-US1180
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                                   19990120
CLASS
 PATENT NO.
                  CLASS PATENT FAMILY CLASSIFICATION CODES
                  ICM
                          A61K047-48
    This invention pertains to a sustained release complex of one or more
     peptides, one or more proteins or a combination thereof immobilized on an
     absorbable polymer microparticle optionally having an absorbable polymer
     coating. The microparticle complex of this invention comprises a
     peptide(s) and/or protein(s) which have at least one amino group and/or at
     least one carboxyl group per mol. and a solid absorbable polyester
     microparticle having surface and subsurface carboxylic group or amino
     groups in sufficient amts. to bind the peptide(s) and/or protein(s) so
     that the immobilized peptide(s) or protein(s) represent 0.1 % to 30 % of the total mass of the microparticle complex. The microparticle complex
     with immobilized peptide(s) and/or protein(s) are optionally further
     encased individually or in groups with an absorbable polymer to control, further, the release of the immobilized peptide(s) and/or protein(s). To
     control the release of the immobilized peptide(s) and/or protein(s) even
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further, the encased microparticles can be incorporated into a composition with

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an absorbable gel-forming liquid that transforms to a flexible gel or
     semi-solid upon contacting water in the biol. environment.
ST
     sustained release microparticle hormone peptide
     Drug delivery systems
IT
         (microparticles; sustained-release microparticles of hormones)
     Enkephalins
     Hormones, animal, biological studies
     Interferons
     Peptides, biological studies
     Proteins, general, biological studies
     Tachykinins
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
         (sustained-release microparticles of hormones)
IT
     Drug delivery systems
         (sustained-release; sustained-release microparticles of hormones)
TT
     62683-29-8, Colony stimulating factor
     RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
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         (granulocyte- or granulocyte-macrophage-; sustained-release
         microparticles of hormones)
     58-82-2, Bradykinin 77-92-9D, Citric acid, reaction products with
                 502-97-6D, Glycolide, reaction products with lactide and
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                                                 119418-04-1, Galanin
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     137061-48-4, Pituitary adenylate cyclase activating peptide
     182153-96-4
                    234752-57-9 234760-89-5, biological studies
     biological studies
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         (sustained-release microparticles of hormones)
               THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 5
RE
(1) Corbett, J; HCAPLUS
(2) Corbett, J; PROC INT SYMP CONTROLLED RELEASE BIOACT MATER 1998, V25TH, P38
(3) Enzytech Inc; WO 9211844 A 1992 HCAPLUS
(4) Ruxandra, G; WO 9503356 A 1995 HCAPLUS
(5) Sandoz Ag; EP 0626170 A 1994 HCAPLUS
L14 ANSWER 13 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
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     131:134660
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     Entered STN: 10 Aug 1999
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     Process for making absorbable microparticles
     Loughman, Thomas Ciaran
IN
     Kinerton Limited, Ire.
PA
SO
     PCT Int. Appl., 32 pp.
     CODEN: PIXXD2
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LA
     English
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     A61K047-48
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     63-6 (Pharmaceuticals)
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                                                 APPLICATION NO.
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CLASS
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                 CLASS PATENT FAMILY CLASSIFICATION CODES
  ...... ....
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 WO 9938535
                         A61K047-48
                  ECLA A61K047/48K4D; A61K047/48K6; A61K047/48W8
 US 6555156
     This invention pertains to a process for making an encased bound
     microparticle sustained release complex comprising one or more peptides,
     one or more proteins or a combination thereof immobilized on an absorbable
     polymer microparticle having an absorbable polymer coating, where the
     process comprises nebulizing a dispersion of the bound microparticles.
     Polyglycolic acid was dispersed in an aqueous solution containing
     p-Glu-His-Trp-Ser-Tyr-D-Trp-Leu-Arg-Pro-Gly-NH2 (LHRH analog) and
     incubated at room temperature for 2 h. The polypeptide-loaded polymers were
     dispersed in acetonitrile solns. of encasing copolymers, e.g.
     glycolide-lactide copolymer. The dispersion was nebulized into isopropanol at -80.degree.. Once nebulization was complete, the entire
     dispersion was allowed to thaw to room temperature The encased microparticles
     were recovered by vacuum filtration over a filter paper. The filter cake
     was rinsed with water, then lyophilized. The obtained bound or encased
     microparticles were administered to rats by i.m. injection to assess the
     release rate of the peptide.
     polyester peptide immobilization microparticle controlled release; LHRH
ST
     analog polyglycolate dispersion nebulization
     Proteins, specific or class
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (biol. active; manufacture of absorbable encased polyester microparticles
        containing biol. active peptides by nebulization)
     Anion exchangers
IT
     Atomizing (spraying)
     Cation exchangers
        (manufacture of absorbable encased polyester microparticles containing biol.
        active peptides by nebulization)
     Enkephalins
     Interferons
     Polyesters, biological studies
     Tachykinins
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (manufacture of absorbable encased polyester microparticles containing biol.
        active peptides by nebulization)
IT
     Drug delivery systems
        (microparticles, controlled-release; manufacture of absorbable encased
        polyester microparticles containing biol. active peptides by nebulization)
    .26009-03-0P, Polyglycolide 26202-08-4P, Polyglycolide 156187-33-6P
IT
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     study); PREP (Preparation); USES (Uses)
        (manufacture of absorbable encased polyester microparticles containing biol.
        active peptides by nebulization)
     58-82-2, Bradykinin 1393-25-5, Secretin 9002-60-2, ACTH, biological studies 9002-64-6, Parathyroid hormone 9002-71-5, TSH 9002-72-6,
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     Calcitonin 9007-92-5, Glucagon, biological studies 9034-39-3, Growth
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     copolymer 31362-50-2, Bombesin 33507-63-0, Substance P 37221-79-7,
     Vasoactive intestinal peptide 39379-15-2, Neurotensin 51110-01-1, Somatostatin 52305-30-3, L-Lactide-DL-lactide copolymer 52906-92-0,
     Motilin 57773-63-4 80043-53-4, Gastrin-releasing peptide 82785-45-3,
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              THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Conti, B; JOURNAL OF MICROENCAPSULATION 1992, V9/2, P153
(2) Enzytech Inc; WO 9211844 A 1992 HCAPLUS
(3) Reyderman, L; Novel methods of microparticulate production:application to
    drug deliver HCAPLUS
(4) Reyderman, L; PHARM DEV TECHNOL 1996, V1(3), P223 HCAPLUS
(5) Ruxandra, G; WO 9503356 A 1995 HCAPLUS
L14 ANSWER 14 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     1998:744968 HCAPLUS
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     130:837
     Entered STN: 24 Nov 1998
ED
     Method of treating hyperprolactinemia and prolactinomas using somatostatin
TI
     type-5 receptor agonists
     Melmed, Shlomo; Shimon, Ilan; Culler, Michael D.
IN
     Cedars-Sinai Medical Center, USA; Biomeasure Inc.
PΑ
     PCT Int. Appl., 26 pp.
SO
     CODEN: PIXXD2
DT
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     English
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     ICM A61K038-31
     ICS A61K038-31; A61K031-48
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     2-5 (Mammalian Hormones)
     Section cross-reference(s): 1
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                       A61K038/31; A61K038/31
 US 5972893
                 ECLA
                 ECLA
                        A61K038/31
 EP 1332762
     A method of treating hyperprolactinemia in an animal, including a human,
     by administering one or more somatostatin type-5 receptor agonist(s) to,
     for example, lower abnormally high levels of prolactin in the blood of the animal. A method of treating a subject, including a human, afflicted by a
     prolactinoma, by administering one or more type-5 receptor selective
     agonist(s) to, for example, lower prolactin secretion and/or decrease
     tumor size in the subject.
     hyperprolactinemia prolactinoma treatment somatostatin receptor agonist
     Somatostatin receptors
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (SSTR5, agonists; method of treating hyperprolactinemia and
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Search done by Noble Jarrell

prolactinomas using somatostatin type-5 receptor agonists)

Audet 09/870087

TΤ Pituitary gland (adenoma, anterior, prolactinoma; method of treating hyperprolactinemia and prolactinomas using somatostatin type-5 receptor agonists) IT (chest wall trauma; method of treating chest wall trauma associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) Pituitary gland TТ (disease, pituitary stalk disease; method of treating hypothalamic or pituitary stalk disease associated with high levels of prolactin using somatostatin type-5 receptor agonists) TT Lactation (disorder, galactorrhea; method of treating galactorrhea associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) IT Fertility (disorder; method of treating infertility associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) IT Kidney, disease (failure; method of treating renal failure or cirrhosis associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) Lactation (galactorrhea; method of treating galactorrhea associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) Reproductive organ IT (hypergonadism; method of treating hypergonadism associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) IT Brain, disease (hypothalamus; method of treating hypothalamic or pituitary stalk disease associated with high levels of prolactin using somatostatin type-5 receptor agonists) Sexual behavior IT (impotence; method of treating impotence associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) IT Kidney, disease (interstitial nephritis; method of treating renal failure or cirrhosis associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) IT Amenorrhea (method of treating amenorrhea associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) ΙT Estrogens RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method of treating decreased dopamine or dopamine inhibitory action associated with high levels of serum prolactin using estrogen) Antitumor agents (method of treating hyperprolactinemia and prolactinomas using somatostatin type-5 receptor agonists) IT (method of treating hyperprolactinemia associated with postpartum lactation using somatostatin type-5 receptor agonists) TT Drugs Psychotropics (method of treating hyperprolactinemia induced by drugs using somatostatin type-5 receptor agonists) TТ Opioids RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (method of treating hyperprolactinemia induced by drugs using somatostatin type-5 receptor agonists) IT Hyperthyroidism (method of treating hyperthyroidism associated with high levels of prolactin using somatostatin type-5 receptor agonists) IТ Anticonvulsants Seizures (method of treating seizures associated with high levels of serum prolactin using somatostatin type-5 receptor agonists) Pituitary gland, anterior lobe (prolactinoma; method of treating hyperprolactinemia and prolactinomas using somatostatin type-5 receptor agonists) IT 9002-62-4, Prolactin, biological studies RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(hyperprolactinemia; method of treating hyperprolactinemia and prolactinomas using somatostatin type-5 receptor agonists)

Page 26 Audet 09/870087

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   51-61-6, Dopamine, biological studies
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                            25614-03-3, Bromocriptine 66104-22-1, Pergolide
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    18016-80-3, Lisuride
     81409-90-7, Cabergoline
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        (method of treating hyperprolactinemia and prolactinomas using
        somatostatin type-5 receptor agonists in combination with other
        therapeutic agents)
RE.CNT
             THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Biomeasure Incorporated; WO 9711962 A 1997 HCAPLUS
(2) Shimon, I; THE JOURNAL OF CLINICAL INVESTIGATION 1997, V100(9), P2386
   HCAPLUS
(3) Shimon, I; THE JOURNAL OF CLINICAL INVESTIGATION 1997, V99(4), P789 HCAPLUS
(4) The Administrators Of The Tulane University Educational Fund; US 4650787 A
   HCAPLUS
(5) The Administrators Of The Tulane University Educational Fund; US 4725577 A
   HCAPLUS
(6) The Administrators Of The Tulane University Educational Fund; EP 0203031 A
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L14 ANSWER 15 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
    1998:394351 HCAPLUS
AN
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     129:68033
    Entered STN: 27 Jun 1998
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ΤI
     Preparation of somatostatin antagonists containing D-amino acids in the
     second position
     Morgan, Barry; Murphy, William; Coy, David H.
IN
     Biomeasure Incorporated, USA; Administration of the Tulane
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     Educational Fund; Morgan, Barry; Murphy, William; Coy, David H.
SO
     PCT Int. Appl., 54 pp.
     CODEN: PIXXD2
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     English
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     ICM C07K007-00
     34-3 (Amino Acids, Peptides, and Proteins)
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AB The invention features somatostatin antagonists I [A1 = D- or L-amino acid residue, or is deleted; A2 = D-Cys, D-penicillamine (D-Pen), aromatic D-amino acid, aliphatic D-amino acid; A3 = aromatic amino acid; A4 = Trp, D-Trp; A6 = Thr, Thr(CH2Ph), Gly, Ser, aliphatic amino acid; A7 = Cys, Pen, aromatic amino acid, aliphatic amino acid; A7 = D- or L- Thr, D- or L-Ser, aromatic D- or L-amino acid, aliphatic D- or L-amino acid; R1, R2 = independently H, (un) substituted lower alkyl, aryl, aryl lower alkyl, heterocyclyl, heterocyclyl lower alkyl, E1SO2, E1CO; E1 = aryl, aryl lower alkyl, heterocyclyl, heterocyclyl lower alkyl; R3 = OH, NH2, C1-12 alkoxy, NHYCH2Z; Y = C1-12 hydrocarbon moiety; Z = H, OH, CO2H, CONH2; or R3 and the carbonyl group of A8 are reduced to form H, lower alkyl, hydroxy lower alkyl; with provisos] having a D-amino acid at the second residue. H-.beta.-Nal-D-Cys-Pal-D-Trp-Lys-Val-Cys-.beta.-Nal-NH2 cyclic disulfide [II; .beta.-Nal = 3-(2-naphthyl)alanine; Pal = 3-(3-pyridyl)alanine] was prepared by standard solid-phase methods on a benzhydrylamine-polystyrene resin using tert-butoxycarbonyl (Boc) N.alpha.-protection. II inhibited the in vitro release of growth hormone in a rat pituitary assay with IC50 = 0.01 .mu.M.

ST somatostatin analog solid phase prepn activity; growth hormone release inhibitor somatostatin analog

IT 51110-01-1, Somatostatin

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(antagonists; preparation of D-amino acid-containing somatostatin antagonists) 111857-93-3P 152045-42-6P 171894-24-9P 195520-46-8P 205234-44-2P 205234-45-3P 205234-46-4P 205234-47-5P 205234-48-6P 205234-49-7P 205234-50-0P 205234-51-1P 205234-54-4P 205234-55-5P 205234-56-6P 205234-58-8P 205234-59-9P 205234-60-2P 205234-61-3P 205234-62-4P 205234-63-5P 205234-65-7P 205234-66-8P 205234-67-9P 205234-69-1P 205234-70-4P 205234-71-5P 205234-68-0P 205237-53-2P 205234-72-6P 205234-73-7P 205234-74-8P 205234-76-0P 209005-80-1P 209005-81-2P 209005-82-3P 209005-83-4P 209005-84-5P 209005-85-6P 209005-86-7P 209005-87-8P 209005-88-9P 209005-89-0P 209005-90-3P 209005-91-4P 209005-93-6P 209005-95-8P 209005-97-0P 209005-99-2P 209006-02-0P 209006-03-1P 209006-01-9P 209006-04-2P 209006-05-3P 209006-06-4P 209006-07-5P 209006-08-6P 209006-09-7P 209006-10-0P 209006-11-1P 209006-12-2P 209006-13-3P 209006-14-4P 209006-15-5P 209006-16-6P 209006-17-7P 209006-18-8P 209006-19-9P 209006-20-2P 209006-21-3P 209006-22-4P 209006-23-5P 209006-24-6P 209006-25-7P 209006-26-8P 209006-27-9P 209006-28-0P 209006-29-1P 209006-30-4P 209006-31-5P 209006-32-6P 209006-33-7P 209006-34-8P 209006-35-9P 209006-36-0P 209006-37-1P 209006-38-2P 209006-39-3P 209006-40-6P 209006-41-7P 209006-42-8P 209006-43-9P 209006-44-0P 209006-45-1P 209006-46-2P 209006-47-3P 209006-48-4P 209006-49-5P 209006-50-8P 209006-51-9P 209006-52-0P 209006-53-1P 209006-54-2P 209006-55-3P 209006-57-5P 209006-56-4P 209006-58-6P 209006-59-7P 209006-60-0P 209006-62-2P 209006-64-4P 209006-67-7P 209006-68-8P 209006-65-5P 209006-66-6P 209006-69-9P 209006-70-2P 209006-71-3P 209006-72-4P 209006-73-5P 209006-74-6P 209006-75-7P 209006-76-8P 209006-77-9P 209006-78-0P 209006-79-1P

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        (preparation of D-amino acid-containing somatostatin antagonists)
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     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (preparation of D-amino acid-containing somatostatin antagonists)
L14
    ANSWER 16 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
    1998:323278 HCAPLUS
     129:19689
DN
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    Entered STN: 30 May 1998
    Acylated cyclodextrin derivatives and their uses in drug supports
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IN
     Shalaby, Shalaby W.; Corbett, Joel Thomas
     Poly-Med, USA; Shalaby, Shalaby W.; Corbett, Joel Thomas
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    PCT Int. Appl., 19 pp.
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     63-6 (Pharmaceuticals)
    Section cross-reference(s): 44
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CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
                         C08B037-16
 WO 9820044
                 ICM
                 ICS
                         A61K047-48
 WO 9820044
                 ECLA
                         A61K047/48W18B; C08B037/00M2B
                         A61K047/48K8B; C08B037/00M2B
US 5916883
                 ECLA
OS MARPAT 129:19689
     A cyclodextrin derivative is disclosed wherein at least 60% of the free
     hydroxy groups of said cyclodextrin are acylated with acyl groups where at
     least one of said acyl groups comprise a free carboxylic group which is
     grafted with hydroxy acids or lactones, e.g., glycolide. The cyclodextrin
     derivative is useful for supporting drug agents, particularly those bearing
     ionogenic amino groups, via ionic bondings. Thus, acetylating a
     beta.-cyclodextrin with Ac2O and succinic anhydride, grafting the
     resulting acylated product with glycolide and lactide, and mixing with
     Decapeptyl gave a supported polypeptide.
     polypeptide acylated cyclodextrin conjugate manuf; drug support
     cyclodextrin acylated deriv
IT
     Drugs
        (acylated cyclodextrin derivs. and uses in drug support)
     Peptides, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (acylated cyclodextrin derivs. and uses in drug support)
     9007-12-9, Calcitonin 9034-40-6, LHRH 51110-01-1, Somatostatin
IT
     57773-63-4, Decapeptyl 108736-35-2, Lanreotide
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (acylated cyclodextrin derivs. and uses in drug support)
     207620-85-7P. 207620-86-8P 207620-87-9P 207620-88-0P
     RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic
     preparation); PREP (Preparation); RACT (Reactant or reagent)
         (intermediates; acylated cyclodextrin derivs. and uses in drug support)
     207620-89-1P, .beta.-Cyclodextrin glutarate propionate-glycolide-lactide
     graft copolymer 207620-90-4P 207620-91-5P 207620-92-6P
     RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
        (supports; acylated cyclodextrin derivs. and uses in drug support)
RE.CNT 4
              THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Parmerter, S; US 3453260 A 1969 HCAPLUS
(2) Sandoz; GB 2145422 A 1985 HCAPLUS
(3) Uda; US 4670419 A 1987 HCAPLUS
(4) Zhong-Yao, S; CARBOHYDRATE RESEARCH 1990, V201(2), P241
     ANSWER 17 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     1998:163467 HCAPLUS
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     128:226683
     Entered STN: 19 Mar 1998
ED
     Method of inhibiting fibrosis with a somatostatin agonist
ΤI
     Culler, Michael D.; Kasprzyk, Philip G.
IN
     Biomeasure Incorporated, USA; Culler, Michael D.; Kasprzyk,
PA
     Philip G.
so
     PCT Int. Appl., 61 pp.
     CODEN: PIXXD2
DΤ
     Patent
LA
     English
IC
     ICM A61K038-00
     2-5 (Mammalian Hormones)
CC
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             LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US,
              UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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19980305

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    WO 1997-US14154
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CLASS
PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
WO 9808529
                 ICM
                        A61K038-00
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    MARPAT 128:226683
    The present invention relates to a method of inhibiting fibrosis in a
AB
     patient. The method comprises administering a therapeutically effective
     amount of a somatostatin, a somatostatin agonist or a pharmaceutically
     acceptable salt thereof to said patient.
ST
     fibrosis inhibition somatostatin agonist
    Kidney, disease
IT
        (HIV; method of inhibiting fibrosis with a somatostatin agonist)
TT
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR1; method of inhibiting fibrosis with a somatostatin agonist)
IT
    Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR2; method of inhibiting fibrosis with a somatostatin agonist)
IT
    Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR3; method of inhibiting fibrosis with a somatostatin agonist)
     Somatostatin receptors
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR4; method of inhibiting fibrosis with a somatostatin agonist)
     Somatostatin receptors
IT
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR5; method of inhibiting fibrosis with a somatostatin agonist)
TT
    Transplant rejection
        (allograft rejection, fibrotic disorder in the kidney; method of
        inhibiting fibrosis with a somatostatin agonist)
     Fibrosis
        (autoimmune; method of inhibiting fibrosis with a somatostatin agonist)
    Nervous system
IT
        (central, disease, fibrosis; method of inhibiting fibrosis with a
        somatostatin agonist)
IT
     Kidney, disease
        (diabetic nephropathy; method of inhibiting fibrosis with a
        somatostatin agonist)
IT
     Cardiovascular system
     Digestive tract
        (disease, fibrosis; method of inhibiting fibrosis with a somatostatin
        agonist)
IT
    Gland
        (endocrine, fibrosis; method of inhibiting fibrosis with a somatostatin
        agonist)
IT
     Eosinophilia
        (eosinophilia-myalgia syndrome; method of inhibiting fibrosis with a
        somatostatin agonist)
IT
     Chemotherapy
     Radiation
     Wound
        (fibrosis from; method of inhibiting fibrosis with a somatostatin
        agonist)
IT Immune system
        (fibrosis induced by an immune reaction; method of inhibiting fibrosis
        with a somatostatin agonist)
     Bone, disease
     Eye, disease
     Kidney, disease
Liver, disease
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Lung, disease
     Skin, disease
     Skin, disease
        (fibrosis; method of inhibiting fibrosis with a somatostatin agonist)
     Fibrosis
IT
        (from an environmental or industrial factor; method of inhibiting
        fibrosis with a somatostatin agonist)
TT
    Kidney, disease
        (glomerulonephritis; method of inhibiting fibrosis with a somatostatin
        agonist)
IT
     Fibrosis
        (idiopathic; method of inhibiting fibrosis with a somatostatin agonist)
IT
     Cirrhosis
     Fibrosis
     Granulation tissue
     Keloid
     Wound
        (method of inhibiting fibrosis with a somatostatin agonist)
    Myeloproliferative disorders
IT
        (myelofibrosis; method of inhibiting fibrosis with a somatostatin
IT
     Human immunodeficiency virus 1
        (nephropathy; method of inhibiting fibrosis with a somatostatin
        agonist)
IT
     Vein
        (occlusion, liver; method of inhibiting fibrosis with a somatostatin
        agonist)
IT
    Skin, disease
        (scar; method of inhibiting fibrosis with a somatostatin agonist)
IT
     Nervous system
        (sclerosis; method of inhibiting fibrosis with a somatostatin agonist)
IT
    Liver, disease
        (veno-occlusive disease; method of inhibiting fibrosis with a
        somatostatin agonist)
IT
     95244-38-5
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
        (demethod of inhibiting fibrosis with a somatostatin agonist)
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        (method of inhibiting fibrosis with a somatostatin agonist)
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              THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Coy; US 4904642 A 1990 HCAPLUS
(2) Tsukamoto; Endocrine Journal 1994, V41(4) MEDLINE
L14 ANSWER 18 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1998:163466 HCAPLUS
ΔN
DN
    128:213736
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Entered STN: 19 Mar 1998
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     Method of inhibiting fibrosis with a somatostatin agonist
     Culler, Michael D.; Kasprzyk, Philip G.
IN
PA
     Biomeasure Incorporated, USA; Culler, Michael D.; Kasprzyk,
     Philip G.
so
     PCT Int. Appl., 24 pp.
     CODEN: PIXXD2
DT
     Patent
     English
LΑ
     ICM A61K038-00
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CC
     2-5 (Mammalian Hormones)
FAN.CNT 3
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             RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
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             GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN,
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CLASS
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os
     MARPAT 128:213736
   The present invention relates to a method of inhibiting fibrosis in a
AB
     patient. The method includes the step of administering a therapeutically
     effective amount of a somatostatin or a somatostatin agonist to said
     patient. The fibrosis can be in the kidney, lung, liver or skin or
     induced by chemotherapy.
     fibrosis inhibition somatostatin
ST
     Somatostatin receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (agonists; method of inhibiting fibrosis with a somatostatin agonist)
IT
     Chemotherapy
        (fibrosis from; method of inhibiting fibrosis with a somatostatin
        agonist)
     Kidney, disease
Liver, disease
IT
     Lung, disease
     Skin, disease
     Skin, disease
        (fibrosis; method of inhibiting fibrosis with a somatostatin agonist)
IT
    Fibrosis
        (method of inhibiting fibrosis with a somatostatin agonist)
IT
     181650-80-6, BIM 23268
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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IT
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
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        (method of inhibiting fibrosis with a somatostatin agonist)
RE.CNT 3
              THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Coy; US 4904642 A 1990 HCAPLUS
(2) Tracy; American Journal of Pathology 1993, V143(6), P1574 HCAPLUS
(3) Tsukamoto; Endocrine Journal 1994, V41(4), P437 MEDLINE
L14 ANSWER 19 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1997:756950 HCAPLUS
DN
    127:351265
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ED
     Entered STN: 04 Dec 1997
ΤI
     Sustained-release ionic conjugate comprising biodegradable polymer and a
     free amino group-containing drug
     Ignatious, Francis; Loughman, Thomas Ciaran; Shalaby,
IN
     Shalaby W.; Touraud, Franck Jean-claude
PΑ
    Kinerton Ltd., Ire.; Ignatious, Francis; Loughman, Thomas
    Ciaran; Shalaby, Shalaby W.; Touraud, Franck Jean-Claude PCT Int. Appl., 23 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
LA
     A61K009-16; A61K047-48
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CC
     63-6 (Pharmaceuticals)
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                                                                     DATE
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             SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM,
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PRAI IE 1996-308
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                                 19960423
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CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                IC
                        A61K009-16IC
                                          A61K047-48
AB A method of spherifying a sustained-release ionic conjugate which contains
     a free carboxyl group-containing biodegradable polymer and a free amino
     group-containing drug which are ionically bonded to each other is disclosed.
     Thus, 18.0 q L-lactic acid-glycolic acid-D,L-malic acid copolymer was
     dissolved in 180 g of acetone followed by addition of 14.4 mL of 0.5 NaOH and
     a solution of 4.28 g of lanreotide acetate in a 50:50 mixture of water:acetone
     and stirred for 2 h to obtain a polymer-peptide ionic conjugate (PPIC).
     The above PPIC solution was slowly added to a 0 degree. water to precipitated PPIC
     as small solid particles were then separated, washed and lyophilized. The specific area of particles was 18.64 m2/g and 90% for the particles has
     diameter >62 .mu.m.
     sustained release ionic conjugate biodegradable polymer; polylactide
ST
     polyglycolide lanreotide sustained release pharmaceutical
TТ
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (biodegradable; sustained-release ionic conjugate comprising
        biodegradable polymer and free amino group-containing drug)
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates; sustained-release ionic conjugate comprising biodegradable
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polymer and free amino group-containing drug) Fats and Glyceridic oils, biological studies IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sesame; sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) Particle size (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) IT Alcohols, uses RL: NUU (Other use, unclassified); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) IT Paraffin oils RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) IT Peptides, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) Polyesters, biological studies TT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) Polysiloxanes, biological studies IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) IT Drug delivery systems (sustained-release; sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) Fats and Glyceridic oils, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (vegetable; sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) 67-63-0, Isopropyl alcohol, uses 67-64-1, Acetone, uses 75-05-8, Acetonitrile, uses 109-99-9, Tetrahydrofuran, uses 110-54-3, Hexane, 110-71-4, Glyme 111-65-9, Octane, uses 141-78-6, Ethyl acetate, 142-82-5, Heptane, uses RL: NUU (Other use, unclassified); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) TT 69-65-8, Mannitol 77-92-9D, Citric acid, polyester containing Tartaric acid, polyester containing, biological studies 110-15-6D, Succinic acid, polyester containing 110-94-1D, Glutaric acid, polyester containing 6915-15-7D, Malic acid, polyester containing 9034-40-6, Lhrh 26009-03-0, Polyglycolide 26023-30-3, Poly[oxy(1-methyl-2-oxo-1,2-ethanediyl)] 26100-51-6, Polylactic acid 26124-68-5, Polyglycolic acid 26202-08-4, Polyglycolide 26680-10-4, Polylactide 29223-92-5, Poly p-dioxanone 31852-84-3, Polytrimethylene carbonate 50862-75-4, Poly(oxycarbonyloxy-1,3-propanediyl) 51110-01-1, Somatostatin 127984-74-1,
Lanreotide acetate 133881-21-7 198418-98-3, biological studies RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (sustained-release ionic conjugate comprising biodegradable polymer and free amino group-containing drug) L14 ANSWER 20 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN 1997:261093 HCAPLUS AN DN 126:301921 Entered STN: 23 Apr 1997 ED Proliferative response of human and animal tumors to surgical wounding of TI normal tissues: onset, duration and inhibition AII Bogden, A. E.; Moreau, J-P.; Eden, P. A. Biomeasure Inc., Milford, MA, 01757-3650, USA SO British Journal of Cancer (1997), 75(7), 1021-1027 CODEN: BJCAAI; ISSN: 0007-0920 PB Churchill Livingstone DT Journal English 2-5 (Mammalian Hormones) Section cross-reference(s): 14 Acceleration of secondary tumor growth and metastases following excision AR of a primary tumor has been attributed to the consequent removal of primary tumor-generated inhibitory factors. However, the authors' studies have shown that surgical wounding of normal tissues significantly stimulated the growth of malignant tissues without the concomitant

presence or excision of a tumor mass. A humoral stimulating component was indicated by the proliferative response of tumors and metastases distant from the surgical wound. All 16 human and murine tumors, of nine different histologies, showed a measurable acceleration of growth when implanted in surgically treated animals, suggesting that the ability of malignant tissue to respond to surgical wounding of normal tissue was not histol. or species specific. The proliferative surge of malignant tissues was detectable soon after wounding and had a duration of 2-3 days. The surgical wound as the source of the tumor-stimulating factor(s) was affirmed by the significant inhibition of tumor proliferative responses when a somatostatin analog was applied topically to the surgical wound within 1 h of wounding, and/or during the critical tumor-stimulatory period of 1-2 days after wounding. A potential therapeutic window for reducing a risk factor that may be inadvertently imposed upon every surgical/oncol. patient is indicated. lanreotide surgery tumor growth

ST

Neoplasm Surgery

(proliferative response of human and animal tumors to surgical wounding of normal tissues: onset, duration and inhibition)

IT Growth factors, animal

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (proliferative response of human and animal tumors to surgical wounding of normal tissues: onset, duration and inhibition)

51110-01-1D, Somatostatin-14, analogs 108736-35-2, Lanreotide IT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (proliferative response of human and animal tumors to surgical wounding of normal tissues: onset, duration and inhibition)

L14 ANSWER 21 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN 1997:101609 HCAPLUS AΝ DN 126:108933 Entered STN: 13 Feb 1997 Ionic molecular conjugates of N-acylated derivatives of poly(2-amino-2-deoxy-D-glucose) and polypeptides IN Shalaby, Shalaby W.; Jackson, Steven A.; Ignatious, Francis; Moreau, Jacques-Pierre UŠA PA PCT Int. Appl., 20 pp. SO CODEN: PIXXD2 DT Patent LA English ICM A61K038-00 IC

63-6 (Pharmaceuticals)

Section cross-reference(s): 33, 34

FAN.CNT 3

	PATENT NO.										APPLICATION NO.					DATE			
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			SG,	SI															
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PRAI	AI US 1995-468947				Α		1995	0606											
		1996				W			0524										
CLAS	S																		

PATENT NO. CLASS PATENT FAMILY CLASSIFICATION CODES

\_\_\_\_\_\_ WO 9639160 ICM A61K038-00 A pharmaceutical composition comprising an N-acylated copolymer and a polypeptide, said polypeptide comprising at least one effective ionogenic amine wherein at least 50 percent of said polypeptide present in said composition is ionically bound to said polymer, is disclosed. The N-acylated copolymer-polypeptide conjugates are useful for the controlled-release of polypeptides. An aqueous soln.of N-succinylated chitosan potassium salt (I) (preparation given) was mixed with an aqueous solution of somatostatin acetate (Somatuline) (II) and stirred until I.II conjugate was precipitated, which was filtered and dried under vacuum. ST polyaminodeoxyglucose polypeptide conjugate; chitosan somatostatin conjugate prepn pharmaceutical Drug delivery systems IT (ionic mol. conjugates of N-acylated derivs. of poly(aminodeoxyglucose) and polypeptides) IT Peptides, reactions RL: RCT (Reactant); RACT (Reactant or reagent) (ionic mol. conjugates of N-acylated derivs. of poly(aminodeoxyglucose) and polypeptides) 64-19-7, Acetic acid, reactions 108-30-5, Succinyl anhydride, reactions 9012-76-4, Chitosan 51110-01-1, Somatostatin 127984-74-1, IT Somatuline RL: RCT (Reactant); RACT (Reactant or reagent) (ionic mol. conjugates of N-acylated derivs. of poly(aminodeoxyglucose) and polypeptides) 9012-76-4DP, Chitosan, acetylated and succinylated, conjugates with IT 51110-01-1DP, Somatostatin, conjugates with polypeptides polypeptides 127984-74-1DP, Somatuline, conjugates with acetylated and succinylated chitosan RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (ionic mol. conjugates of N-acylated derivs. of poly(aminodeoxyglucose) and polypeptides) L14 ANSWER 22 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN AN 1996:695866 HCAPLUS DN 126:14869 Entered STN: 25 Nov 1996 ED Potent somatostatin analogs containing N-terminal modifications TΙ Kim, S. H.; Dong, J. Z.; Gordon, T. D.; Kimball, H. L.; Moreau, S. C.; AU Moreau, J.-P.; Morgan, B. A.; Murphy, W. A.; Taylor, J. E. Biomeasure, Inc., Milford, MA, 01757, USA CS Peptides: Chemistry, Structure and Biology, Proceedings of the American SO Peptide Symposium, 14th, Columbus, Ohio, June 18-23, 1995 (1996), Meeting Date 1995, 241-243. Editor(s): Kaumaya, Pravin T. P.; Hodges, Robert S. Publisher: Mayflower Scientific, Kingswinford, UK. CODEN: 63NTAF DT Conference LΑ English CC 2-2 (Mammalian Hormones) The clin. utility of somatostatin analogs such as Octreotide and Lanreotide is now well established. Recent reports on the improved bioavailability of various peptides with certain N- or C-terminal modifications prompted us to investigate the discovery of a second generation of somatostatin analogs with greater potency in vivo. Our efforts were focused on N-terminal modification of cyclic octapeptides related to somatostatin. We now report the design, synthesis, and aspects of the in vitro and in vivo activities of these analogs. ST somatostatin analog N terminal modification 83150-76-9, Octreotide 108736-35-2, TT 51110-01-1, Somatostatin Lanreotide 119719-11-8, Ilatreotide 150155-55-8, BIM-23060 168016-90-8, BIM-23197 182153-96-4, BIM-23190 182494-55-9, BIM 23167 182494-58-2, BIM 23182 182494-57-1, BIM 23179 182494-56-0, BIM 23173 182494-62-8, BIM 23196 182494-59-3, BIM 23201 182494-60-6, BIM 23195 184356-62-5, BIM 23180 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study) (potent somatostatin analogs containing N-terminal modifications) L14 ANSWER 23 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN 1996:563655 HCAPLUS AN DN. 125:276578 ED Entered STN: 21 Sep 1996 Ascorbic acid, tris, and piperazine peptide derivatives as antitumor,

growth hormone release inhibiting, and thymidine uptake stimulating agents

```
Kim, Sun H.; Keyes, Susan R.; Moreau, Sylviane; Dong, Zheng X.; Taylor,
IN
     John
PA
     Biomeasure, Inc., USA
     U.S., 45 pp., Cont.-in-part of U. S. 104,194, abandoned.
so
     CODEN: USXXAM
DT
     Patent
     English
LA
     ICM C07K005-00
IC
     ICS C07K007-00; C07K017-00
NCL
     530311000
     34-3 (Amino Acids, Peptides, and Proteins)
CC
     Section cross-reference(s): 2, 63
FAN.CNT 2
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                         KIND
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                                            APPLICATION NO.
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                                19950626
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                                19940808
CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
PATENT NO.
                 ICM
                        C07K005-00
 US 5552520
                 ICS
                        C07K007-00; C07K017-00
                        530311000
                 NCL.
EP 1288223
                 ECLA
                        C07K007/08D
   MARPAT 125:276578
GI
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II

A peptide derivative is claimed, consisting of: a biol. active peptide having a free amino group, and at least one substituent attached to said peptide selected from the group consisting of I-III wherein: for I, R0 is, e.g., O, S; each R1 and R2 is independently H, (CH2) mOR6, or CH(OR7) CH2OR8, wherein R6 is H or (C2-C7) acyl, and each R7 and R8, independently, is, e.g., H, (C2-C7) acyl; m is an integer between 1 and 5, inclusive; one of R3 and R4 is (CH2) nR12 or (CH2) nCH(OH) R12, wherein R12 is CO, CH2 or SO2, and n is an integer between 1 and 5, inclusive; and the other of R3 and R4 is H, (C1-C6) hydroxyalkyl, or (C2-C7) acyl; for II, each R13, R14, and R15, independently, is H or (C2-C24) acyl; R16 is NH or absent; R17 is CO, O, or absent; R18 is CO, CH2, SO2, or absent; m is an integer between 1 and 5, inclusive; n is an integer between 1 and 5, inclusive; for III, R19 is, e.g., H, NH2, an aromatic functional group, OH; R20 is O or absent; R21 is (C1-C6) alkyl or absent; R22 is N, O, C, or CH; R23 is (C1-C6) alkyl or absent; R24 is N, CH, or C; R25 is NH, O, or absent; R26 is SO2, CO, or CH2; m is an integer between 0 and 5, inclusive; n is an integer between 0 and 5, inclusive; p is an integer between 0 and 5, inclusive; and q is an integer between 0 and 5, inclusive; wherein said peptide is attached to said substituent at R12, R18, or R26 via an amide, amino, or sulfonamide bond. Thus, e.g., amide coupling of D-Nal-Cyclo-[Cys-Tyr-D-Trp-Lys(BOC)-Val-Cys]-Thr-NH2 (preparation given) with 3-O-(carboxypropyl)-5,6isopropylideneascorbic acid (preparation given) followed by deprotection afforded somatostatin derivative IV (BIM-23118) which exhibited IC50 = 0.30 nM for binding to the somatostatin receptor and antiproliferative activity (cell growth = 61.0% of control after 8 days) at 100 nM using rat pancreas tumor cells vs. 91.3 and 98.0% of control, resp., for SRIF-14 and SRIF-28 (unmodified somatostatin analogs). Data are also presented for bombesin binding assay of a bombesin analog, inhibition of release of growth hormone by somatostatin analogs (in which all derivs. demonstrate a surprising prolonged duration of action which decreases in a time-dependent fashion), and thymidine uptake stimulation by bombesin analogs. peptide ascorbate tris piperazine deriv therapeutic; somatostatin analog antitumor growth hormone inhibitor; bombesin analog thymidine uptake

ST stimulation

IT Receptors

> RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(GRP; ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating agents)

IT Neoplasm inhibitors

(ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating agents)

IT Peptides, preparation

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(analogs, ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating agents)

TT Receptors

RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(somatostatin, ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating agents)

TТ 168016-90-8P, BIM 23197 182153-96-4P 182494-49-1P, BIM 23118 182494-50-4P, BIM 23135 182494-51-5P, BIM 23181 182494-52-6P, BIM 23183 182494-53-7P, BIM 23107 182494-54-8P, BIM 23158 182494-55-9P, BIM 23167 182494-56-0P, BIM 23173 182494-57-1P. BIM 23179 182494-58-2P, BIM 23182 182494-59-3P, BIM 23201 182494-60-6P, BIM 23195 182494-61-7P, BIM 23191 182494-62-8P, BIM 182494-63-9P, BIM 23202 182494-64-0P, BIM 26333 23196 BTM 23109

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating agents)

50-89-5, Thymidine, biological studies 9002-72-6, Growth hormone IT RL: BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study)

(ascorbic acid, tris, and piperazine peptide derivs. as antitumor,

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growth hormone release inhibiting, and thymidine uptake stimulating
        agents)
     50-81-7, Ascorbic acid, reactions 67-64-1, 2-Propanone, reactions
TΤ
     103-76-4, 1-(2-Hydroxyethyl)piperazine 2969-81-5, Ethyl 4-bromobutyrate 4263-52-9, Sodium 2-bromoethanesulfonate 13051-30-4 24424-99-5,
     Di-tert-butyl dicarbonate 108736-35-2, BIM-23014 168016-98-6
     168017-02-5 182482-14-0
                                   182482-16-2
     RL: RCT (Reactant); RACT (Reactant or reagent)
         (ascorbic acid, tris, and piperazine peptide derivs. as antitumor,
        growth hormone release inhibiting, and thymidine uptake stimulating
     15042-01-0P 54429-56-0P, 2-Bromoethanesulfonyl chloride
168016-91-9P 168016-92-0P 168016-05 (2016)
IT
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     182482-11-7P 182482-12-8P 182482-13-9P
                    182482-17-3P
     182482-15-1P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (ascorbic acid, tris, and piperazine peptide derivs. as antitumor, growth hormone release inhibiting, and thymidine uptake stimulating
        agents)
L14 ANSWER 24 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
AN
     1996:544511 HCAPLUS
DN
     125:257040
     Entered STN: 12 Sep 1996
TΙ
     Improved analogs and novel delivery systems for somatostatin octapeptides
     Moreau, J.-P.; Kim, S.; Dong, J. Z.; Ignatious, F.;
ΑU
     Jackson, S.; Moreau, S. C.; Morgan, B. A.; Touraud, F.; Taylor, J.
     E.: et al.
CS
     Biomeasure Inc., Milford, MA, 01757-3650, USA
     Metabolism, Clinical and Experimental (1996), 44(8, Suppl. 1), 24-26
SO
     CODEN: METAAJ; ISSN: 0026-0495
PB
     Saunders
DT
     Journal
     English
LA
CC
     63-6 (Pharmaceuticals)
AB
     Appropriate N-terminus modification can result in somatostatin (SRIF)
     octapeptide analogs that are both more potent and more selective in vitro
     for the human SRIF receptor type 2 (hsst2). In addition, these modifications can improve the duration of action and bioavailability of SRIF analogs
     following parenteral administration, as shown by both pharmacol. and
     distribution studies in vivo with BIM-23190 and BIM-23197 in the rat.
ST
     somatostatin octapeptide analog delivery system
IT
     Drug bioavailability
     Pharmaceutical dosage forms
        (improved analogs and novel delivery systems for somatostatin
        octapeptides)
TT
     38916-34-6, Somatostatin (sheep)
                                          51110-01-1D, Somatostatin, analogs
     83150-76-9, Octreotide 108736-35-2, Lanreotide 150155-54-7,
                  150155-55-8, BIM-23060
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     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (improved analogs and novel delivery systems for somatostatin
        octapeptides)
L14 ANSWER 25 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1995:806295 HCAPLUS
AΝ
DN
     123:228909
     Entered STN: 22 Sep 1995
     Preparation of therapeutic peptide derivatives.
TΙ
     Kim, Sun Hyuk; Dong, Zhengxin; Taylor, John E.; Moreau, Sylviane; Keyes,
IN
     Susan Riley
PA
     Biomeasure, Inc., USA.
     PCT Int. Appl., 47 pp.
SO
     CODEN: PIXXD2
DT
     Patent
     English
          C07K005-04
     ICM
          C07K007-10; C07K007-34; C07K007-36; C07K007-44; C07K007-26;
     ICS
           C07K007-38; C07K007-12; A61K037-24; A61K037-28; A61K037-40
CC
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
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                                                                        DATE
                                                                         19940808
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                        C07K007-10; C07K007-34; C07K007-36; C07K007-44;
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                        C07K007-26; C07K007-38; C07K007-12; A61K037-24;
                        A61K037-28; A61K037-40
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                        C07K007/08D
EP 1288223
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                           (CH<sub>2</sub>)
                 R130-CH2
                R14OCH2C (CH2) mR16R17 (CH2) pR18
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R150CH2

N(CH<sub>2</sub>)<sub>2</sub>SO<sub>2</sub>-D-Phe-Cys-Tyr-D-Trp-Lys-Abu-Cys-Thr-NH<sub>2</sub>

(CH<sub>2</sub>)<sub>2</sub>OH

Page 41

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Peptide derivs. containing .gtoreq.1 of Q1, Q2, Q3 [X = O, S, NR5; R5 = H,
     alkyl; R1, R2 = H, (CH2)mOR6, CH(OR7)CH2OR8; R6, R13, R15 = H, acyl; R7, R8 = H, acyl, CR9R10; R9 = H, alkyl; R1R2 = :CHCH2OR11; R11 = H, acyl; m, n = 1-5; one of R3, R4 = (CH2)nR12, (CH2)nCH(OH)R12, the other = H,
     hydroxyalkyl, acyl; R12 = CO, CH2, SO2; R16 = HN, null; R17 = CO, O, null;
     R18 = CO, CH2, SO2, null; p, q, r, s = 0-5; R19 = H, NH2, aromatic functional group, OH, hydroxyalkyl, SO3H, null, etc.; R20 = O, null; R21 = alkyl,
     null; R22 = N, O, C, CH; R23 = alkyl, null; R24 = N, CH, C; R25 = NH, O,
     null; R26 = SO2, CO, CH2, null] attached to the peptide by a CO-N, CH2-N,
     or SO2-N bond, were prepared Thus, somatostatin deriv (I) (solution phase
     preparation given) at 100 nM in AR42J pancreas tumor cells gave 66.4% control
     of cell growth.
     peptide analog prepn neoplasm inhibitor; somatostatin deriv prepn drug;
     bombesin deriv prepn drug
     Enkephalins
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
     BIOL (Biological study); PREP (Preparation); USES (Uses)
         (derivs; preparation of therapeutic peptide derivs.)
ΤT
     Neoplasm inhibitors
         (preparation of therapeutic peptide derivs.)
     Peptides, preparation
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         (preparation of therapeutic peptide derivs.)
     58-82-2DP, Bradykinin, derivs. 9002-60-2DP, Adrenocorticot hormone, derivs. 9002-64-6DP, Parathyroid hormone, derivs.
                                          9002-60-2DP, Adrenocorticotrophic
     9002-72-6DP, Somatotropin, derivs. 9002-76-0DP, Gastrin, derivs.
     9002-79-3DP, Melanocyte stimulating hormone, derivs. Calcitonin, derivs. 9007-92-5DP, Glucagon, derivs.
                                                                   9007-12-9DP,
                                                                   9011-97-6DP
     Cholecystokinin, derivs. 9034-39-3DP, Growth hormone releasing factor,
                9034-40-6DP, Luteinizing hormone releasing hormone, derivs.
     33507-63-0DP, Substance P, derivs. 37221-79-7DP, Vasoactive intestinal
     peptide, derivs. 51110-01-1DP, Somatostatin, derivs.
                                                                      75788-99-7DP.
      beta.-Cell tropin, derivs. 80043-53-4DP, Gastrin-releasing peptide,
                82785-45-3DP, Neuropeptide Y, derivs. 83652-28-2DP, Calcitonin
     gene related peptide, derivs. 96352-57-7DP, Glucagon-like peptide,
               103370-86-1DP, Humoral hypercalcemic factor, derivs.
     105953-91-1DP, Neuromedin, derivs. 106388-42-5DP, Peptide YY, derivs.
     106602-62-4DP, Amylin, derivs. 116243-73-3DP, Endothelin, derivs.
     137061-48-4DP, Pituitary adenylate cyclase activating polypeptide, derivs.
     144940-98-7DP, Guanylin, derivs. 148440-40-8DP, derivs. 150155-54-7DP, derivs. 154835-90-2DP, Adrenomedullin, derivs.
     168016-87-3P 168016-88-4P 168016-89-5P
                                                     168016-90-8P
     168017-03-6DP, derivs. 168017-04-7P
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     50-81-7, L-Ascorbic acid, reactions 103-76-4, N-2-Hydroxyethylpiperazine 2969-81-5, Ethyl 4-bromobutyrate 91353-57-0 168016-98-6
                                   168017-01-4 168017-02-5
     168016-99-7 168017-00-3
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42-01-0P 54429-56-0P 126100-72-9P 168016-91-9P
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     15042-01-0P
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     168016-97-5P
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
         (preparation of therapeutic peptide derivs.)
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     123:188934
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     Entered STN: 14 Sep 1995
     Somatostatin (SSTR2) receptors mediate phospholipase C-independent Ca2+
TI
     mobilization in rat AR42J pancreas cells
ΑU
     Taylor, John E.
     Biomeasure Inc., Milford, MA, 01757, USA
CS
so
     Biochemical and Biophysical Research Communications (1995), 214(1), 81-5
```

CODEN: BBRCA9; ISSN: 0006-291X

Academic

Journal

English

DT

LΑ

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CC
    2-5 (Mammalian Hormones)
     Rat AR42J pancreas cells, which express somatostatin-SSTR2 type receptors,
     responded to SSTR2-selective somatostatin (SRIF) agonist ligands with a
     dose-dependent increase in intracellular Ca2+. In addition to SRIF-14 and
     SRIF-28, the most potent SRIF peptides were the cyclic octapeptides,
     BIM-23014C, BIM-23023, SMS 201-995, and the cyclic hexapeptides, MK-678
     and BIM-23027. The SSTR3 and SSTR5-selective ligands, BIM-23056 and
     BIM-23052, were inactive and weakly active, resp. None of the SRIF peptides stimulated inositol phosphate turnover, indicating that Ca2+
     mobilization was independent of phospholipase C activation. Incubation in
     calcium-free medium abolished the increase in intracellular Ca2+. These
     results indicate that activation of SSTR2 receptors in AR42J cells opens
     cell-surface calcium channels.
     somatostatin SSTR2 receptor calcium pancreas
ST
     Signal transduction, biological
TT
        (somatostatin SSTR2 receptors mediation of phospholipase C-independent
        calcium mobilization in rat AR42J pancreas cells)
IT
     Receptors
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (SSTR2 (somatostatin receptor 2), somatostatin SSTR2 receptors
        mediation of phospholipase C-independent calcium mobilization in rat
        AR42J pancreas cells)
TТ
     Pancreas
        (acinar cell, somatostatin SSTR2 receptors mediation of phospholipase
        C-independent calcium mobilization in rat AR42J pancreas cells)
IT
     Ion channel
        (calcium, somatostatin SSTR2 receptors mediation of phospholipase
        C-independent calcium mobilization in rat AR42J pancreas cells)
IT
     Biological transport
        (channel-mediated, somatostatin SSTR2 receptors mediation of
        phospholipase C-independent calcium mobilization in rat AR42J pancreas
        cells)
     51110-01-1, Somatostatin-14
                                   73032-94-7, Somatostatin-28 (sheep)
     81377-02-8, MK-678 83150-76-9, SMS 201-995 121715-55-7, BIM-23027
     127984-74-1, BIM-23014C 150155-54-7, BIM 23023
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); BIOL (Biological study)
        (somatostatin SSTR2 receptors mediation of phospholipase C-independent
        calcium mobilization in rat AR42J pancreas cells)
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     7440-70-2, Calcium, biological studies 9001-86-9, Phospholipase C
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
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        (somatostatin SSTR2 receptors mediation of phospholipase C-independent
        calcium mobilization in rat AR42J pancreas cells)
IT
     68247-19-8, myo-Inositol phosphate
     RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
        (somatostatin SSTR2 receptors mediation of phospholipase C-independent
        calcium mobilization in rat AR42J pancreas cells)
L14 ANSWER 27 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1994:692773 HCAPLUS
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                   24 Dec 1994
     Inhibition of trauma-induced tumor growth with somatostatin and
TI
     somatostatin agonists
IN
     Bodgen, Arthur E.; Moreau, Jacques-Pierre
     Biomeasure, Inc., USA
so
     PCT Int. Appl., 33 pp.
     CODEN: PIXXD2
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IC
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     ICS C07K007-00; C07K007-06; C07K007-26; C07K007-64; A61K037-02
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EP 644893

A1

19950329

19940208

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                         C07K005-12
                         C07K007-00; C07K007-06; C07K007-26; C07K007-64;
                         A61K037-02
 US 5504069
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                         A61K038/31
    A method for inhibiting in a mammal the accelerated growth of a solid
     primary or metastatic tumor resulting from tissue trauma caused
     surgically, non-surgically, or by tissue ulceration, comprises the step of administering to the mammal a therapeutically effective amount of somatostatin or a somatostatin agonist. Mice in which prostate tumor,
     breast tumor, or malignant melanoma cells had been implanted were
     subjected to surgical trauma. The trauma stimulated growth of the tumor. When the somatostatin agonist BIM-23014 was applied to the tumor area, the
     tumors produced following surgical trauma weighed 22-43% less.
ST
     tumor growth trauma induced inhibition somatostatin
IT
     Neoplasm inhibitors
         (inhibition of trauma-induced tumor growth with somatostatin and '
        somatostatin agonists)
     Neoplasm inhibitors
IT
         (colon, inhibition of trauma-induced tumor growth with somatostatin and
        somatostatin agonists)
TT
     Intestine, neoplasm
        (colon, inhibitors, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
     Neoplasm inhibitors
IT
         (epithelium, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
     Lung, neoplasm
        (inhibitors, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
IT
     Neoplasm inhibitors
        (lung, inhibition of trauma-induced tumor growth with somatostatin and
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IT
     Neoplasm inhibitors
         (mammary gland, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
IT
     Neoplasm inhibitors
         (melanoma, inhibition of trauma-induced tumor growth with somatostatin
        and somatostatin agonists)
IT
     Neoplasm inhibitors
         (metastasis, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
IT
     Epithelium
     Mammary gland
        (neoplasm, inhibitors, inhibition of trauma-induced tumor growth with
        somatostatin and somatostatin agonists)
IT
        (trauma, inhibition of trauma-induced tumor growth with somatostatin
        and somatostatin agonists)
TT
     51110-01-1, Somatostatin 108736-35-2, BIM-23014
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (inhibition of trauma-induced tumor growth with somatostatin and
        somatostatin agonists)
    ANSWER 28 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
L14
AN
     1994:612977 HCAPLUS
DN
     121:212977
ED
     Entered STN: 29 Oct 1994
TI
     Ionic molecular conjugates of biodegradable polyester and bioactive
     polypeptides
IN
     Shalaby, Shalaby W.; Jackson, Steven A.; Moreau,
     Jacques Pierre
PA
     Kinerton Ltd., Ire.
SO
     PCT Int. Appl., 35 pp.
     CODEN: PIXXD2
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     63-6 (Pharmaceuticals)
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ECLA A61K047/48K6; C07K007/23; C07K014/655
 EP 1203591
 US 6221958
AB A sustained-release pharmaceutical composition includes a bioactive polypeptide
     containing .gtoreq.1 effective ionogenic amine, .gtoreq.50% by weight of which is
     ionically conjugated to a polyester containing a free CO2H group. The ionic
     conjugate release a therapeutically ED of the polypeptide in vivo over a period of .gtoreq.7 days. Thus, an ionic conjugate of [D-Trp6]LHRH with a L-lactic acid/glycolic acid/malic acid (49:49:2) copolymer released 55.2%
     of the peptide in 14 days in phosphate-buffered saline at 37.degree..
     peptide ionic conjugate polyester sustained release
ST
     Enkephalins
IT
     RL: BIOL (Biological study)
         (ionic conjugates with polyesters, sustained-release dosage form
        containing)
     Polyesters, biological studies
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (conjugates, ionic, with peptides, sustained-release dosage form
TT
     Peptides, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (conjugates, ionic, with polyesters, sustained-release dosage form
         containing)
IT
     Particles
         (micro-, of peptide-polyester ionic conjugates, peptide sustained
        release from)
IT
     Pharmaceutical dosage forms
         (sustained-release, peptide ionic conjugates with polyesters)
     Kinins (animal hormones)
IT
     RL: BIOL (Biological study)
         (tachykinins, ionic conjugates with polyesters, sustained-release
         dosage form containing)
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57773-63-4D, ionic conjugates with polyesters 108736-35-2D, ionic conjugates with polyesters 133881-21-7D, ionic conjugate with BIM-23014 133881-21-7D, ionic conjugates with peptides 136207-23-3D, BIM 26226, ionic conjugates with polyesters RL: BIOL (Biological study) (peptide sustained release from) 26780-50-7P, DL-Lactide/glycolide copolymer 30846-39-0P, L-Lactide/glycolide copolymer 34346-01-5P, DL-Lactic acid/glycolic acid 133881-21-7P 158054-05-8P 158054-06-9P copolymer 133881-21-7P RL: PREP (Preparation) (preparation and ionic conjugation with peptides, as sustained-release dosage form) IT 58-82-2D, Bradykinin, ionic conjugates with polyesters Butanedioic acid, polymers with alkylene glycols, ionic conjugates with peptides 142-62-1D, Caproic acid, .epsilon - substituted, polymers, ionic conjugates with peptides 144-62-7D, Ethanedioic acid, polymers with alkylene and cycloalkylene glycols, ionic conjugates with peptides 1393-25-5D, Secretin, ionic conjugates with polyesters 9002-60-2D, ACTH, ionic conjugates with polyesters 9002-64-6D, Parathormone, ionic conjugates with polyesters 9002-71-5D, TSH, ionic conjugates with polyesters 9002-79-3D, MSH, ionic conjugates with polyesters 9007-12-9D, Calcitonin, ionic conjugates with polyesters 9007-92-5D, Glucagon, ionic conjugates with polyesters 9034-39-3D, Growth hormone-releasing factor, ionic conjugates with polyesters 9034-40-6D, LHRH, ionic conjugates with polyesters 24980-41-4D, Poly(.epsilon.caprolactone), ionic conjugates with peptides 25038-75-9D, Poly-D-lactide, ionic conjugates with peptides 25248-42-4D, Poly(.epsilon.-caprolactone), ionic conjugates with peptides 26009-03-0D, Polyglycolide, ionic conjugates with peptides 26023-30-3D, Poly(DL-lactic acid), ionic conjugates with peptides 26063-00-3D, Poly(.beta.-hydroxybutyric acid), ionic conjugates with peptides 26100-51-6D, Poly(DL-lactic acid), ionic conjugates with peptides 26161-42-2D, Poly(L-lactic acid), ionic conjugates with peptides 26202-08-4D, Polyglycolide, ionic conjugates with peptides 26680-10-4D, Poly-DL-lactide, ionic conjugates with peptides 26811-96-1D, Poly(L-lactic acid), ionic conjugates with peptides 26917-25-9D, Poly(D-lactic acid), ionic conjugates with peptides 29223-92-5D, Poly(p-dioxanone), ionic conjugates with peptides 31362-50-2D, Bombesin, ionic conjugates with polyesters 31852-84-3D, Poly(trimethylene carbonate), ionic conjugates with peptides 33507-63-0D, Substance P, ionic conjugates with polyesters 37221-79-7D, Vasoactive intestinal peptide, ionic conjugates with polyesters 39379-15-2D, Neurotensin, ionic conjugates with polyesters 50862-75-4D, Poly(trimethylene carbonate), ionic conjugates with peptides 51110-01-1D, Somatostatin, ionic conjugates with polyesters 52906-92-0D, Motilin, ionic conjugates with polyesters 80043-53-4D, Gastrin-releasing peptide, ionic conjugates with polyesters 82785-45-3D, Neuropeptide Y, ionic conjugates with polyesters 83652-28-2D, Calcitonin gene-related peptide, ionic conjugates with polyesters 85205-36-3D, Glucagon-releasing factor, ionic conjugates with polyesters 103370-86-1D, Parathormone-related protein, ionic conjugates with polyesters 105953-91-1D, Neuromedin, ionic conjugates with polyesters 106388-42-5D, Peptide YY, ionic conjugates with polyesters 106602-62-4D, Amylin, ionic conjugates with polyesters 119418-04-1D, Galanin, ionic conjugates with polyesters 121425-66-9 ionic conjugates with peptides 121425-79-4D, ionic conjugates with 121425-66-9D, peptides 137061-48-4D, Pituitary adenylate cyclase-activating peptide, ionic conjugates with polyesters 158054-04-7D, ionic conjugates with peptides 227186-48-3D, Poly-meso-lactide, ionic conjugates with peptides RL: BIOL (Biological study) (sustained-release dosage form containing) L14 ANSWER 29 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN AN 1993:617391 HCAPLUS DN 119:217391 Entered STN: 27 Nov 1993 ED ΤI Hepatoma treatment with somatostatin analogs Bogden, Arthur E. IN PA Biomeasure, Inc., USA SO PCT Int. Appl., 19 pp. CODEN: PIXXD2

DT

LA IC Patent English

ICM A61K037-02

1-6 (Pharmacology)

ICS C07K005-12; C07K007-06; C07K007-08

Section cross-reference(s): 2, 34

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CLASS
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                        C07K005-12; C07K007-06; C07K007-08
                        A61K038/31; C07K014/655A
US 5411943
                 ECLA
OS MARPAT 119:217391
     Hepatomas in mammals are treated by administering octapeptide somatostatin
     analogs A1-Cys-A2-D-Trp-Lys-A3-Cys-A4-Y [A1 = D-.beta.-Nal; D-Phe; A2 =
     Phe, pentafluoro-Phe, p-substituted X-Phe (X = halo, NH2, NO2, OH, C1-3
     alkyl); A3 = Thr, Ser, Phe, Val, .alpha.-aminobutyric acid, Ile; A4 = Thr, .beta.-Nal, Trp; Y = NH2, OH] or acceptable salts or complexes.
     D-.beta.-Nal-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2, prepared by solid phase synthesis on benzhydrylamine-polystyrene resin, inhibited the growth of
     M5123 hepatomas in mice.
     hepatoma inhibitor somatostatin analog
ST
IT
     Neoplasm inhibitors
        (hepatoma, somatostatin analogs as)
     Liver, neoplasm
IT
        (hepatoma, inhibitors, somatostatin analogs as)
                   145758-77-6 150957-55-4 150957-56-5 150996-95-5
IT
     103548-90-9
     150996-96-6
     RL: BIOL (Biological study)
     (hepatoma inhibitor)
51110-01-1D, Somatostatin, analogs
TΤ
     RL: BIOL (Biological study)
        (hepatoma inhibitors)
     2389-45-9 3978-80-1
                             5241-64-5 13734-41-3 15260-10-3 61925-77-7
IT
     76985-10-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (peptide coupling reaction of, in preparation of hepatoma inhibitor)
IT
     113294-90-9DP, benzyhydrylamine resin-bound
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation and deprotection and cleavage of, from resin, in preparation of
        hepatoma inhibitor)
TT
     113294-82-9P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as hepatoma inhibitor)
L14
    ANSWER 30 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1993:806 HCAPLUS
AN
DN
     118:806
ED
     Entered STN: 10 Jan 1993
     Method of treating benign and malignant proliferative skin disease by
ΤI
     topical administration of a somatostatin analog
TN
     Bogden, Arthur E.; Moreau, Jacques Pierre
     Biomeasure, Inc., USA
PA
     PCT Int. Appl., 25 pp.
SO
     CODEN: PIXXD2
DT
     Patent
LA
     English
     ICM A61K037-02
IC
     1-6 (Pharmacology)
     Section cross-reference(s): 2, 34, 63
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                                             APPLICATION NO.
                                                                     DATE
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     WO 9213554
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                                 19920820
                                              WO 1992-US1027
                                                                      19920207
         W: CA, CS, FI, HU, JP, NO, RU
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Page 47

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                                19930526
                                            EP 1992-906420
                                                                    19920207
                              19990616
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                          B1
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                                19930916
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                          Т3
                                19991016
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                                                                    19920207
     ES 2134798
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                                            US 1993-89410
                                                                    19930709
                          Α
PRAI US 1991-652863
                          Α
                                19910208
     WO 1992-US1027
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                                19920207
CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
 PATENT NO.
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                ICM
                        A61K037-02
WO 9213554
os
    MARPAT 118:806
    A composition for treating a mammal suffering from benign or malignant
AB
     proliferative skin disease comprises an effective amount of a somatostatin
     analog containing .gtoreq.6 amino acids, formulated with an excipient suitable
     for topical administration to the mammal. D-.beta.-Naphthyl-Ala-Cys-Tyr-D-
     Trp-Lys-Val-Cys-Thr-NH2 was synthesized on benzhydrylamine-polystyrene
     resin. B16-F10 melanoma xenografts in mice were treated with topical
     somatuline.
     skin proliferative disease somatostatin analog; somatuline melanoma
ST
     inhibitor
IT
     Neoplasm inhibitors
        (melanoma, topical somatuline as)
IT
     Skin, disease
        (proliferative, treatment of, with topical somatostatin analog)
IT
     Pharmaceutical dosage forms
        (topical, of somatostatin analogs, for treatment of benign or malignant
        proliferative skin disease)
     51110-01-1D, Somatostatin, analogs 77236-35-2 81377-02-8 99660-13-6
TT
     103222-11-3 108736-35-2
                              144776-53-4
                                            144831-72-1
     RL: BIOL (Biological study)
        (benign or malignant proliferative skin disease topical treatment with)
                3978-80-1 5241-64-5 13734-41-3 15260-10-3 61925-77-7
     2389-45-9
IT
     76985-10-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (coupling reaction of, in somatostatin analog synthesis)
     113294-82-9P
IT
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, for treatment of benign or malignant proliferative skin
        disease)
IT
     9003-53-6D, Benzhydrylamine derivs.
     RL: BIOL (Biological study)
        (somatostatin analog synthesis on)
    ANSWER 31 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
L14
AN
     1991:599065 HCAPLUS
     115:199065
DN
ED
     Entered STN: 15 Nov 1991
     Octapeptide analogs of somatostatin inhibit the clonal growth and
     vasoactive intestinal peptide-stimulated cyclic AMP formation in human
     small cell lung cancer cells
     Taylor, J. E.; Moreau, J. P.; Baptiste, L.; Moody, T. W.
ΑU
     Biomeasure Inc., Hopkinton, MA, 01748, USA
CS
     Peptides (New York, NY, United States) (1991), 12(4), 839-43
SO
     CODEN: PPTDD5; ISSN: 0196-9781
DT
     Journal
LΑ
     English
     2-5 (Mammalian Hormones)
CC
     Section cross-reference(s): 14
     Two endocrinol. active octapeptide analog (BIM-23014 C and BIM-23034) of
     somatostatin (SRIF) containing either an N- or C-terminal 3-(2-naphthyl)-D-Ala
     residue were examined for their ability to inhibit the in vitro receptor
     binding, clonal growth, and VIP-stimulated cAMP formation in human small
     cell lung cancer cell (SCLC) line NCI-H345. Both SRIF peptides inhibited
     [1251] SRIF (Tyr11) -14 binding with IC50 values in the low nM range. Colony
     formation in the in vitro SCLC growth assay was also inhibited in the same
     concentration range, as was VIP-stimulated cAMP formation. Therefore, octapeptide analogs of SRIF function as SCLC SRIF receptor agonists.
     somatostatin analog lung cancer cell; receptor somatostatin analog lung
ST
     cancer; VIP cAMP lung cancer somatostatin
IT
     Receptors
     RL: BIOL (Biological study)
        (somatostatin octapeptide analogs binding by, in small cell lung
```

carcinoma, proliferation inhibition in relation to) Neoplasm inhibitors IT (carcinoma, somatostatin octapeptide analogs as, in human lung, receptor binding and VIP-stimulated cAMP formation in relation to) Lung, neoplasm IT (small-cell carcinoma, cAMP formation by, of human, VIP stimulation of, octapeptide somatostatin analogs inhibition of, receptor binding in relation to) 51110-01-1D, Somatostatin, octapeptide analogs 111857-95-5, BIM 23034 IT 127984-74-1 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (antitumor activity of, in human small cell lung carcinoma, receptor binding and VIP-induced cAMP formation in relation to) 37221-79-7, VIP TT RL: BIOL (Biological study) (cAMP formation stimulation by, in human small cell lung carcinoma, somatostatin octapeptide analogs inhibition of) 60-92-4, CAMP TT RL: FORM (Formation, nonpreparative) (formation of, VIP stimulation of, in human small cell lung carcinoma, somatostatin octapeptide analogs inhibition of) L14 ANSWER 32 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN 1991:136284 HCAPLUS AN DN 114:136284 Entered STN: 19 Apr 1991 ED Comparison of somatuline (BIM-23014) and somatostatin on endocrine and ΤI exocrine activities in the rat Moreau, Sylviane C.; Murphy, William A.; Coy, David H. Biomeasure Inc., Hopkinton, MA, 01748, USA AU CS Drug Development Research (1991), 22(1), 79-93 SO CODEN: DDREDK; ISSN: 0272-4391 DT Journal English LA CC 2-5 (Mammalian Hormones) The actions of Somatuline (BIM-23014), an octapeptide analog of somatostatin, and somatostatin have been compared on several endocrine and exocrine activities in the rat. A substantial difference exists between these 2 compds. with respect to potency, duration of action, and tissue selectivity. With regard to endocrine activities, Somatuline was about 300 times more potent than somatostatin in inhibiting growth hormone (GH) release 15 min after i.v. injection, and about 4 to 6 times more potent 15 min after s.c. administration. The inhibitory activity of s.c. administered Somatuline on D-Ala2-GRF-stimulated GH release lasted for about 6 h, whereas an action of somatostatin was not detected 30 min after injection. Somatuline was also more potent than somatostatin in inhibiting insulin-stimulated glucagon secretion when both substances were administered i.v., whereas they were about equipotent when given by the s.c. route. However, Somatuline was only about half as potent as somatostatin by the i.v. route in inhibiting glucose-stimulated insulin release and was inactive by the s.c. route. With regard to exocrine activities, Somatuline was about 300-500 times more potent than somatostatin in inhibiting the increase in plasma .alpha.-amylase activity following ligation-induced pancreatitis when both compds. were administered s.c. concurrently with pancreatic duct ligation. Somatuline was also about 20-400 times more potent that somatostatin in inhibiting gastric acid secretion when both compds. were administered s.c. prior to, or concurrently with, pentagastrin challenge and about 100 times more potent than somatostatin when administered after pentagastrin challenge. Somatuline had a very weak inhibitory effect on the development of ethanol-induced gastric ulcers, it did not induce diarrhea, and it had no effect on the course of diarrhea in rats subjected to castor oil gavage. The differences between Somatuline and somatostatin indicate the Somatuline may be more useful in treating certain disease states. Somatuline somatostatin biol activity; pancreas function Somatuline ST somatostatin; digestive tract function Somatuline somatostatin; growth hormone release Somatuline somatostatin IT Stomach, metabolism (acid secretion by, Somatuline inhibition of, somatostatin in relation to) IT 38916-34-6. Somatostatin RL: BIOL (Biological study) (endocrine and exocrine activities response to, Somatuline in relation

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IT
     127984-74-1, Somatuline
     RL: BIOL (Biological study)
        (endocrine and exocrine activities response to, somatostatin in
        relation to)
                                   9004-10-8, Insulin, biological studies
     9002-72-6, Growth hormone
     9007-92-5, Glucagon, biological studies
     RL: BIOL (Biological study)
         (release of, Somatuline inhibition of, somatostatin in relation to)
IT
     9000-90-2, .alpha.-Amylase
     RL: BIOL (Biological study)
        (secretion of, by pancreas, Somatuline inhibition of, somatostatin in
        relation to)
L14 ANSWER 33 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1991:82559 HCAPLUS
AN
     114:82559
DN
     Entered STN: 09 Mar 1991
     Preparation of octapeptideamides as hormone release inhibitors or
ΤI
     antagonists
IN
     Eck, Charles R.; Moreau, Sylvianne
     Biomeasure, Inc., USA
PA
     Eur. Pat. Appl., 8 pp.
     CODEN: EPXXDW
рΤ
     Patent
LΑ
     English
     ICM C07K007-06
IC
     ICS A61K037-02; C07K007-26
ICI C07K099-60
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 2
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     EP 389180
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                                  19900926
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     CA 2012115
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PRAI US 1989-323777
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                                  19890315
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                  TCM
                         A61K037-02; C07K007-26
                  ICS
                         C07K099-60
                  ICI
OS
     MARPAT 114:82559
     R1R2NCHR3CO-Cys-Tyr(I)-D-Trp-Lys-X1-Cys-XNH2 [R1 ,R2 = H, alkyl,
AΒ
     phenylalkyl, acyl, (phenyl)alkoxycarbonyl; R3 = CH2R4, R4 = pentafluorophenyl, naphthyl, pyridyl, (substituted) Ph; Tyr(I) = Tyr ring-iodinated at the 3- or 5-position; X1 = Thr, Ser, Phe, Val, Ile,
     .alpha.-aminobutyryl; X2 = Thr, Trp, .beta.-Nal], were prepared as drugs (no
     data). Thus, D-.beta.-naphthylalanyl-Cys-Tyr(I)-D-Trp-Lys-Val-Cys-Thr-NH2
     was prepared using Me3CO2C-protected amino acids on benzhydrylamine resin
     followed by iodination with chloramine T/NaI in pH 7.4 phosphate buffer.
     octapeptideamide prepn drug; hormone release inhibitor octapeptideamide
ST
     Antidiabetics and Hypoglycemics
     Neoplasm inhibitors
     Nervous system agents
     Ulcer inhibitors
         (octapeptideamides)
IT
     Acromegaly
     Diarrhea
     Liver, disease or disorder
         (treatment of, octapeptides for)
     Eye, disease or disorder
         (diabetic retinopathy, treatment of, octapeptideamides for)
IT
     Peptides, compounds
     RL: SPN (Synthetic preparation); PREP (Preparation)
         (octa-, amides, preparation of, as hormone release inhibitors or
         antagonists)
IT
     Pancreas, disease or disorder
     (pancreatitis, treatment of, octapeptides for)
9002-72-6, Growth hormone 9004-10-8, Insulin, biological studies
IT
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9007-92-5, Glucagon, biological studies
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (antagonists, octapeptideamides)
IT
     51110-01-1P, Somatostatin
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (octapeptide analogs, preparation of, as hormone release inhibitors or
        antagonists)
TT
     108736-35-2P
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     (Reactant or reagent)
        (preparation and iodination of)
     131799-87-6P
TΤ
                    131799-88-7P 131799-89-8P
                                               131799-90-1P
     131799-91-2P
                    131799-92-3P 131799-93-4P 131836-60-7P
     131836-61-8P
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as hormone release inhibitor or antagonist)
IT
     113294-90-9DP, benzhydrylamine resin bound
     RL: SPN (Synthetic preparation); PREP (Preparation)
        (preparation of, as intermediates for hormone secretion inhibitor or
        antagonist)
тт
     96658-24-1D, benzhydrylamine resin bound
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (reaction of, in preparation of hormone secretion inhibitor or antagonist)
     2389-45-9 3978-80-1 5241-64-5
тт
                                        13734-41-3
                                                      61925-77-7 76985-10-9
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (solid-phase peptide coupling of, in preparation of hormone secretion
        inhibitor antagonist)
L14
    ANSWER 34 OF 34 HCAPLUS COPYRIGHT 2004 ACS on STN
     1988:448729 HCAPLUS
AN
DN
     109:48729
     Entered STN: 19 Aug 1988
ED
ΤI
     In vitro and in vivo inhibition of human small cell lung carcinoma
     (NCI-H69) growth by a somatostatin analog
     Taylor, John E.; Bogden, Arthur E.; Moreau, Jacques Pierre; Coy, David H.
AU
     Biomeasure Inc., Hopkinton, MA, 01748, USA
CS
SO
     Biochemical and Biophysical Research Communications (1988), 153(1), 81-6
     CODEN: BBRCA9; ISSN: 0006-291X
DT
     Journal
     English
LА
CC
     2-5 (Mammalian Hormones)
     An endocrinol.-potent octapeptide analog of somatostatin (SRIF),
AB
     3-(2-naphthyl)-D-Ala-Cys-Tyr-D-Trp-Lys-Val-Cys-Thr-NH2 (BIM-23014 C), was
     examined for its ability to inhibit the in vitro and in vivo growth of the
     human small cell lung carcinoma (SCLC) line, NC1-H69. When cultured cells
     were implanted into athymic nude mice, treatment (500 .mu.g/injection,
     twice daily) resulted in a prolongation of lag time for the appearance of
     measurable tumors, and there was a marked inhibition of the growth rate.
     Indeed, peptide injection in the region of the tumor resulted in a
     complete regression of the NCl-H69 tumors. Withdrawal of BIM-23014 C
     treatment resulted in an acceleration of tumor growth indicating an
     antiproliferative rather the oncolytic action. A similar inhibition of
     tumor growth was also observed when solid tumors obtained from the 1st
     implantation were used as the donor tissues. In cell culture, the
     proliferation in the presence of a low concentration (10 nM) of BIM-23104 C was
     also retarded suggesting a direct mechanism of action.
ST
     somatostatin analog antitumor lung carcinoma; neoplasm inhibitor lung
     somatostatin analog
     Neoplasm inhibitors
IT
        (carcinoma, somatostatin analog as, in lung of human)
IT
     Lung, neoplasm
        (small-cell carcinoma, somatostatin analog inhibition of, from human)
IT
     113294-82-9
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (antitumor activity of, in human small-cell lung carcinoma)
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## कारी हारा इस्टार्ट्स विश्व है कि

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L19 ANSWER 1 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
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- AN 2002:276518 HCAPLUS
- DN 136:304089
- ED Entered STN: 12 Apr 2002
- TI Method of treating insulin insensitivity and syndrome X

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Cawthorne, Michael Anthony; Liu, Yong-ling; Sennitt, Matthew V.
IN
PA
SO
    U.S. Pat. Appl. Publ., 15 pp.
    CODEN: USXXCO
\mathbf{DT}
    Patent
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     English
    ICM A61K038-00
IC
     ICS C07K005-00; C07K007-00; C07K016-00; C07K017-00; A61K038-12
NCL
    514015000
CC
    1-10 (Pharmacology)
FAN.CNT 1
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                                                                    DATE
                         KIND
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    PATENT NO.
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    US 2002042374
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                                                                    19980513 <--
PRAI US 1997-46373P
                          P
                                19970513 <--
CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
US 2002042374
                 ICM
                        A61K038-00
                        C07K005-00; C07K007-00; C07K016-00; C07K017-00;
                 ICS
                        A61K038-12
                 NCL
                        514015000
os
    MARPAT 136:304089
    The present invention relates to a method of treating insulin resistance
AR
     or syndrome X in a patient. The method includes the step of administering
     a therapeutically effective amount of a somatostatin or a somatostatin
    agonist to said patient. Among examples provided are: binding of several somatostatin agonists to human somatostatin receptors, improvement of
     insulin sensitivity in BIM-23268-treated fatty Zucker rats, and reduction of
     hypertriglyceridemia by BIM-23268C in obese Zucker rats.
ST
     somatostatin agonist insulin resistance treatment
     Somatostatin receptors
    RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SSTR1; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
     Somatostatin receptors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SSTR2; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
     Somatostatin receptors
IT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SSTR3; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
IT
     Somatostatin receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SSTR4; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
TТ
     Somatostatin receptors
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (SSTR5; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
IT
     Lipids, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (hyperlipidemia; somatostatin and somatostatin agonists in treatment of
        insulin insensitivity and syndrome X)
IT
    Body weight
        (loss; somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
IT
    Disease, animal
        (metabolic syndrome X; somatostatin and somatostatin agonists in
        treatment of insulin insensitivity and syndrome X)
     Hypertriglyceridemia
TT
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
IT
     Glycerides, biological studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
     56-81-5, Glycerol, biological studies
IT
                                              9004-10-8, Insulin, biological
     studies
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
     51110-01-1, Somatostatin-14
                                   75037-27-3, Somatostatin-28
                                                                   83150-76-9.
TT
     Octreotide 108736-35-2, BIM 23014
                                        133073-82-2, BIM 23052
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181650-80-6, BIM 23268
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     216259-69-7, BIM 23313
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
                  72127-59-4
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TΤ
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                  77236-42-1
                                77236-46-5
                                             77286-22-7
                                                           77286-23-8
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                                                           85003-75-4
     79775-25-0
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                                  109790-92-3
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     111857-96-6
                   116861-48-4
                                  117580-23-1
                                                117580-24-2
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                                                 144776-53-4
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     150155-54-7
                   150155-55-8
                                  150155-57-0
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     410069-18-0
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
IT
     108736-35-2, BIM 23014
     RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL
     (Biological study); USES (Uses)
        (somatostatin and somatostatin agonists in treatment of insulin
        insensitivity and syndrome X)
RN
     108736-35-2 HCAPLUS
     L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
CN
     tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide
     (9CI) (CA INDEX NAME)
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ANSWER 2 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
L19
     2001:255236 HCAPLUS
AN
DN
     134:261259
     Entered STN: 11 Apr 2001
     Method using octreotide and an anticholinergic agent for treating acute
TI
     and severe diarrhea
IN
     Simon, David Lew
PA
     USA
     U.S., 5 pp., Cont.-in-part of U.S. Ser. No. 82,260, abandoned.
so
     CODEN: USXXAM
DT
     Patent
     English
LΑ
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ICM A61K038-00
IC
     ICS A61K031-40; A01N043-36
NCL
    514009000
    1-9 (Pharmacology)
     Section cross-reference(s): 2
FAN.CNT 6
                                           APPLICATION NO.
                                                                 DATE
     PATENT NO.
                        KIND DATE
                                -----
                                           -----
                                                                  -----
                                         US 1999-435564
    US 6214792
                         B1
                               20010410
                                                                 19991108 <--
     US 5783583
                         A
                               19980721
                                          US 1996-631081
                                                                 19960412 <--
PRAI US 1996-631081
                         A2
                               19960412 <--
    US 1998-82260
                        B2
                               19980520 <--
CLASS
                CLASS PATENT FAMILY CLASSIFICATION CODES
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                       A61K038-00
                ICM
 US 6214792
                ICS
                       A61K031-40; A01N043-36
                NCL
                       514009000
                ECLA A61K031/485; A61K031/485
US 6214792
   The invention provides a method for treating acute and severe diarrhea,
     such as that which accompanies chemotherapy and rapid narcotic
     detoxification. The method includes administering octreotide in an amount
     sufficient to alleviate the diarrhea without precipitating clin. significant
     bradycardia. In a preferred embodiment an anticholinergic agent is
     administered together with octreotide to further reduce the possibility of
     significant bradycardia. The invention also provides a method for rapidly
     detoxifying a patient addicted to narcotics. Acute and severe diarrhea is
     eliminated during detoxification by administering octreotide in according
     to the above-described method.
    octreotide anticholinergic antidiarreal; chemotherapy antidiarrheal
     octreotide anticholinergic; narcotic detoxification antidiarrheal
     octreotide anticholinergic
    Heart, disease
IT
        (bradycardia; octreotide and anticholinergic agent for treating acute
        and severe diarrhea)
IT
    Heart
        (cardiac postganglionic parasympathetic neuroeffector site; octreotide
        and anticholinergic agent for treating acute and severe diarrhea)
IT
    Drug delivery systems
        (injections, needleless jet injector; octreotide and anticholinergic
        agent for treating acute and severe diarrhea)
TТ
     Drug delivery systems
        (injections, s.c.; octreotide and anticholinergic agent for treating
        acute and severe diarrhea)
TT
    Antidiarrheals
     Cholinergic antagonists
     Muscarinic antagonists
        (octreotide and anticholinergic agent for treating acute and severe
        diarrhea)
IT
    Neurotransmission
        (parasympathetic, cardiac postganglionic parasympathetic neuroeffector
        site; octreotide and anticholinergic agent for treating acute and
        severe diarrhea)
IT
    Drug delivery systems
        (parenterals; octreotide and anticholinergic agent for treating acute
        and severe diarrhea)
     51-55-8, Atropine, biological studies 596-51-0, Glycopyrrolate
IT
     83150-76-9, Octreotide 108736-35-2, Lanreotide
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (octreotide and anticholinergic agent for treating acute and severe
     51-84-3, Acetylcholine, biological studies
     RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
     (Biological study); PROC (Process)
        (octreotide and anticholinergic agent for treating acute and severe
             THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 1
RE
(1) Gooberman; US 5789411 1998 HCAPLUS
     108736-35-2, Lanreotide
     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (octreotide and anticholinergic agent for treating acute and severe
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diarrhea)
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ST

Blood vessel

RN 108736-35-2 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

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ANSWER 3 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
L19
     2001:73387 HCAPLUS
AN
DN
     134:127880
     Entered STN: 01 Feb 2001
ED
     Method to enhance tissue accumulation of radiolabeled compounds
ΤI
IN
     Woltering, Eugene A.; Espenan, Gregory D.
     Board of Supervisors of Louisiana State University and Agricultural and
PA
     Mechanical College, USA
SO
     U.S., 46 pp.
     CODEN: USXXAM
DT
     Patent
     English
LA
IC
     A61K051-00; A61M036-14
     424016900
NCL
     8-9 (Radiation Biochemistry)
CC
     Section cross-reference(s): 63
FAN.CNT 1
                                              APPLICATION NO.
                                                                      DATE
     PATENT NO.
                          KIND
                                 DATE
                                              US 1998-198562
                                                                      19981123 <--
ΡI
     US 6180082
                           В1
                                 20010130
                           B1
                                 20031007
                                              US 2000-664456
                                                                      20000918 <--
     US 6630123
PRAI US 1997-160087P
                           Р
                                 19971124
     US 1998-198562
                           A1
                                 19981123
CLASS
 PATENT NO.
                  CLASS PATENT FAMILY CLASSIFICATION CODES
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 US 6180082
                  IC
                         A61K051-00IC
                                          A61M036-14
                 NCL
                         424016900
                         A61K051/08
 US 6630123 ·
                  ECLA
     Administration of a radioisotopic compound by infusion over a period of time
AB
     greater than two hours, preferably greater than twelve hours, greatly
     increases the maximum radioactivity that accumulates in the target cell.
     Increasing tissue accumulation and retention of radiolabeled compds.
     improves their therapeutic and diagnostic value. The efficacy of the
     administration of the radiolabeled compound can be increased about five
     times higher than prior bolus injection or short infusion methods. This
     method enhances the tumor to background ratio by increasing the actual
     radioligand accumulated inside the target cells. This technique works for
     any radiolabeled compound whose cellular uptake is limited by a cellular
     process of either binding to a cellular receptor or to a transport
     protein. Once the radiolabeled compound is bound and internalized, the
     ability of an unlabeled compound to compete with the radioligand is markedly decreased. The primary factor governing residence time after
     internalization is the phys. half-life of the radioisotope, not biol.
     half-life. Preliminary results of clin. trial with 111In-pentetreotide
     infusions are presented.
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radiopharmaceutical tumor angiogenic tissue accumulation enhancement

Page 55

(angiogenic; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Astrocyte (astrocytoma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Skin, neoplasm (carcinoma, Merkel cell; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Mammary gland (carcinoma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) Blood vessel TT (endothelium; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Neuroglia (glioma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) Pancreatic islet of Langerhans IT (glucagonoma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) ŤΤ Drug delivery systems (infusions; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Thyroid gland, neoplasm (medullary carcinoma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT (meningioma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) Angiogenesis IT Angiogenesis inhibitors Antitumor agents Lymphoma Melanoma Neoplasm Pancreas, neoplasm Pheochromocytoma Scintigraphy (method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) TT Platelet-derived growth factor receptors Somatostatin receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) Estrogens IT Glucocorticoids Gonadotropins Interferons Interleukins Leukemia inhibitory factor Mineralocorticoids Opioids Platelet-derived growth factors Transferrins RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Digestive tract Endocrine system Pancreatic islet of Langerhans Pituitary gland (neoplasm; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Nerve, neoplasm (neuroblastoma; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT DNA RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (nuclear; method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals) IT Peptides, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(radiolabeled receptor-dependent; method for enhancing tumor and

```
angiogenic tissue accumulation of radiopharmaceuticals)
     Steroids, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (receptor-dependent; method for enhancing tumor and angiogenic tissue
         accumulation of radiopharmaceuticals)
IT
     Kidney, neoplasm
         (renal cell carcinoma; method for enhancing tumor and angiogenic tissue
         accumulation of radiopharmaceuticals)
IT
     Lung, neoplasm
         (small-cell carcinoma; method for enhancing tumor and angiogenic tissue
         accumulation of radiopharmaceuticals)
IT
     Imaging
     Paraganglion
         (tumor; method for enhancing tumor and angiogenic tissue accumulation
         of radiopharmaceuticals)
     139096-04-1
     RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or
     effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC
      (Process); USES (Uses)
         (method for enhancing tumor and angiogenic tissue accumulation of
         radiopharmaceuticals)
IT
     50-28-2D, 17.beta.-Estradiol, iodine-125 labeled
                                                               186293-19-6D.
     iodine-125 and iodine-131 labeled
     RL: BPR (Biological process); BSU (Biological study, unclassified); THU
      (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
         (method for enhancing tumor and angiogenic tissue accumulation of
         radiopharmaceuticals)
     50-56-6, Oxytocin, biological studies 57-83-0, Progesterone, biological
IT
               58-22-0, Testosterone 67-43-6D, DPTA, radiolabeled
     somatostatin conjugates 113-79-1, Arginine vasopressin
                                                                         9002-62-4
     Prolactin, biological studies 9002-72-6, Growth hormone
                                                                          9004-10-8,
     Insulin, biological studies 9007-12-9, Calcitonin 9007-92-5, , Glucagon, biological studies 9011-97-6, Cholecystokinin 9015-71-8,
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     Corticotropin-releasing hormone 9034-39-3, Growth hormone-releasing
                                                                  9061-61-4. Nerve
                9034-40-6, Gonadotropin-releasing hormone
     hormone
     growth factor 10043-66-0, Iodine 131, biological studies 10098-91-6,
     Yttrium 90, biological studies 11128-99-7, Angiotensin II 14119-09-6, Gallium 67, biological studies 14133-76-7, Technetium 99, biological studies 14158-30-6, Iodine 124, biological studies 14158-31-7, Iodine
     125, biological studies 14269-78-4, Ytterbium 169, biological studies 14378-26-8, Rhenium 188, biological studies 14809-53-1, Yttrium 86,
     biological studies 15046-84-1, Iodine 129, biological studies
     15715-08-9, Todine 123, biological studies 15750-15-9, Indium 111, biological studies 15765-39-6, Bromine 77, biological studies
     24305-27-9, Thyrotropin-releasing hormone 33507-63-0, Substance P 37221-79-7, Vasoactive intestinal peptide 39379-15-2, Neurotensin
     37221-79-7, Vasoactive intestinal peptide
     51110-01-1, , Somatostatin 51110-01-1D, Somatostatin, analogs
     60239-18-1D, DOTA, radiolabeled somatostatin conjugates
                                                                       62031-54-3.
     Fibroblast growth factor 62229-50-9, Epidermal growth factor
     80043-53-4, Gastrin-releasing peptide 82785-45-3, Neuropeptide Y
     83150-76-9, Octreotide 83150-76-9D, Octreotide, technetium-99 complexes
     85637-73-6, Atrial natriuretic peptide 103222-11-3, Vapreotide 103222-11-3D, RC-160, metal complexes 105953-91-1, Neuromedin
     108736-35-2, Lanreotide 113202-69-0, 125I-Tyr3-octreotide 127464-60-2, Vascular endothelial growth factor 138661-02-6,
                       184584-18-7 186293-19-6 186293-20-9 186293-20-9D,
     Pentetreotide
      iodine-125 and iodine-131 labeled 187810-07-7 189758-24-5
     189758-25-6 213187-48-5 213187-51-0 271785-06-9
      271785-06-9D, iodine-125 and iodine-131 labeled 321983-88-4
                                  321999-23-9
     321983-89-5 321983-90-8
      321999-24-0 321999-25-1
      RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (method for enhancing tumor and angiogenic tissue accumulation of
         radiopharmaceuticals)
RE.CNT 52
                THERE ARE 52 CITED REFERENCES AVAILABLE FOR THIS RECORD
(1) Anon; WO 9101144 1991 HCAPLUS
(2) Barrie, R; Journal of Surgical Research 1993, V55, P446 HCAPLUS
(3) Bloomer, W; Current Topics in Radiation Research Quarterly 1977, V12, P513
(4) Breeman, W; European Journal of Nuclear Medicine 1994, V21(4), P328 HCAPLUS
(5) Breeman, W; Quarterly Journal of Nuclear Medicine 1996, V40, P209 MEDLINE
(6) Carrasquillo, J; The Journal of Nuclear Medicine 1987, V28, P281 MEDLINE
(7) Coy; US 5597894 1997 HCAPLUS
(8) de Jong, M; European Journal of Nuclear Medicine 1997, V24, P368 HCAPLUS
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(9) Dence, C; Nuclear Medicine & Biology 1996, V23, P491 HCAPLUS

- (10) Fjalling, M; Journal of Nuclear Medicine 1996, V37, P1519 MEDLINE
- (11) Hildebrandt, G; Acta Neurochirurgica 1992, V117, P160 MEDLINE
- (12) Hochberg, R; Science 1979, V205, P1138 HCAPLUS (13) Hofland, L; Endocrinology 1995, V136, P3698 HCAPLUS
- (14) Kalofonos, H; The Journal of Nuclear Medicine 1989, V30, P1636 MEDLINE
- (15) Kaplan, W; Journal of Clinical Oncology 1984, V2(11), P1266 MEDLINE
- (16) Kessler, R; The Journal of Nuclear Medicine 1991, V32, P1593 HCAPLUS
- (17) Kolan, H; Peptide Research 1996, V9(3), P144 HCAPLUS
- (18) Krenning, E; Annals of the New York Academy of Sciences 1996, V733, P496
- (19) Krenning, E; European Journal of Nuclear Medicine 1993, V20, P716 MEDLINE
- (20) Krenning, E; The Journal of Nuclear Medicine 1992, V33, P652 MEDLINE
- (21) Krenning, E; The Lancet 1989, V1989(1), P242
- (22) Kurtaran, A; The Journal of Nuclear Medicine 1997, V38, P880 MEDLINE
- (23) Laduron, P; Biochemical Pharmacology 1994, V47, P3 HCAPLUS
- (24) Lamberts, S; The New England Journal of Medicine 1990, V323, P1246 MEDLINE
- (25) Meyers, M; Paper Presented at the Association for Academic Surgery 1998
- (26) Morel, G; Biochemical Pharmacology 1994, V47(1), P63 HCAPLUS
- (27) Nakabeppu, Y; Annals of Nuclear Medicine 1994, V8(4), P259 MEDLINE
- (28) Nouel, D; Endocrinology 1997, V138, P296 HCAPLUS
- (29) O'Dorisio; US 5590656 1997
- (30) O'Reilly, M; Regulation of Angiogenesis 1997, P273 HCAPLUS
- (31) Patel, P; Surgery 1994, V116, P1148 MEDLINE
- (32) Press, O; Cancer Research 1996, V56, P2123 HCAPLUS (33) Reubi, J; International Journal of Cancer 1994, V56, P681 MEDLINE
- (34) Rippley, R; Biophysical Journal 1995, V69, P825 HCAPLUS
- (35) Roberson, P; Supplement to Cancer 1997, V80, P2567 HCAPLUS
- (36) Strand, S; Medical Physics 1993, V20(2)(Pt 2), P515
- (37) Sutherland, D; The Basic Science of Oncology, 2d Ed 1992, P207
- (38) Thakur, M; Nuclear Medicine & Biology 1997, V24, P105 HCAPLUS
- (39) Vanhagen, P; Arthritis & Rheumatism 1994, V37(10), P1521 MEDLINE
- (40) Virgolini, I; Paper Submitted to Journal of Nuclear Medicine 1997
- (41) Virgolini, I; The New England Journal of Medicine 1994, V331, P1116 MEDLINE
- (42) Wang, L; Biochimica et Biophysica Acta 1993, V1175, P232 HCAPLUS
- (43) Watson, J; Paper Presented at the 12th International Symposium on Regulatory Peptides 1996
- (44) Watson, J; Regulatory Peptides 1996, V64, P206
- (45) Watson, J; Surgery 1997, V122, P508 MEDLINE
- (46) Watson, J; Surgical Forum 1996, V47, P462 (47) Welshons, W; Nature 1984, V307, P747 HCAPLUS
- (48) Wiseman, G; Seminars in Nuclear Medicine 1995, VXXV(3), P272 (49) Woltering, E; Investigational New Drugs 1997, V15, P77 HCAPLUS
- (50) Woltering, E; Journal of Surgical Research 1991, V50, P245 HCAPLUS
- (51) Woltering, E; Principles & Practice of Oncology 1995, V9, P1 (52) Zhu, H; The Journal of Nuclear Medicine 1997, V38(5), P731 HCAPLUS
- 108736-35-2, Lanreotide 213187-48-5 213187-51-0
  - 321983-88-4 321983-89-5 321983-90-8
  - 321999-24-0 321999-25-1
  - RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (method for enhancing tumor and angiogenic tissue accumulation of radiopharmaceuticals)
- RN 108736-35-2 HCAPLUS
- L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-CN tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

RN

213187-48-5 HCAPLUS
Indium-111In, [3-(2-naphthalenyl)-N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]-1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]acetyl-.kappa.O]-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide cyclic (2.fwdarw.7)-disulfidato(3-)]- (9CI) (CA INDEX NAME) CN

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PAGE 2-A

PAGE 2-B

CN

RN

213187-51-0 HCAPLUS
Yttrium-90Y, [3-(2-naphthalenyl)-N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl-.kappa.0]-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-Lvalyl-L-cysteinyl-L-threoninamide cyclic (2.fwdarw.7)-disulfidato(3-)]-(9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

PAGE 2-A

11

PAGE 2-B



RN 321983-88-4 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-3-(iodo-125I)-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

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RN 321983-90-8 HCAPLUS

CN L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-3-(iodo-131I)-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide (9CI) (CA INDEX NAME)

RN

321999-24-0 HCAPLUS
Yttrium-86Y, [3-(2-naphthalenyl)-N-[[4,7,10-tris[(carboxy-.kappa.0)methyl]1,4,7,10-tetraazacyclododec-1-yl-.kappa.N1,.kappa.N4,.kappa.N7,.kappa.N10]
acetyl-.kappa.O]-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-Lvalyl-L-cysteinyl-L-threoninamide cyclic (2.fwdarw.7)-disulfidato(3-)](9CI) (CA INDEX NAME) CN

PAGE 1-A

PAGE 1-B

PAGE 2-A

PAGE 2-B

CN

RN

321999-25-1 HCAPLUS
Indate(1-)-111In, [N-[(carboxy-.kappa.0)methyl]-N-[2-[[(carboxy-.kappa.0)methyl] [2-[[(carboxy-.kappa.0)methyl] (carboxymethyl)amino-.kappa.N]ethyl]amino-.kappa.N]ethyl]glycyl-.kappa.N-3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-L-threoninamide cyclic (2.fwdarw.7)-disulfidato(4-)]-, hydrogen (9CI) (CA INDEX NAME)

PAGE 1-A

PAGE 1-B

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ANSWER 4 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
L19
     2000:506101 HCAPLUS
AN
DN
     133:135746
     Entered STN: 26 Jul 2000
ED
     Bioresorbable copolymers based on cyclic carbonates
TI
IN
     Gross, Richard A.; Chen, Xianhai; McCarthy, Stephen P.
     University of Massachusetts, USA
PA
     U.S., 20 pp.
SO
     CODEN: USXXAM
DT
     Patent
     English
LΑ
IC
     ICM C08G063-08
NCL
    528354000
     35-5 (Chemistry of Synthetic High Polymers)
     Section cross-reference(s): 63
FAN.CNT 1
                                                                 , DATE
                                            APPLICATION NO.
     PATENT NO.
                         KIND
                                DATE
                                             ----
                                20000725
                                            US 1998-154332
                                                                    19980916 <--
ΡI
     US 6093792
                          Α
PRAI US 1997-59013P
                          Р
                                19970916 <--
CLASS
 PATENT NO.
                 CLASS PATENT FAMILY CLASSIFICATION CODES
US 6093792
                 ICM
                        C08G063-08
                 NCL
                        528354000
     A bioresorbable copolymer composition comprises products of a reaction between:
     (a) a first comonomer comprising lactones, lactides, lactams,
     thiolactones, or nonfunctionalized cyclic carbonates; and (b) a second,
     functionalized, cyclic carbonate comonomer, wherein the second comonomer
     is functionalized by a substituent group comprising alkenes, alkynes,
     protected hydroxyl groups or protected carboxyl groups. The high mol. weight
     bioresorbable copolymers are useful for specific applications in the
     biomedical arts. A polymer was prepared by polymerization of 2,4-
     dioxaspiro[5.5]undecane-8-ene-3-one and L-lactic acid.
ST
     cyclic carbonate lactone copolymer bioresorbable
IT
     Drug delivery systems
     Polymerization catalysts
        (bioresorbable copolymers based on cyclic carbonates)
IT
     Polyesters, preparation
     Polyesters, preparation
     RL: IMF (Industrial manufacture); PRP (Properties); TEM (Technical or
     engineered material use); PREP (Preparation); USES (Uses)
        (polycarbonate-; bioresorbable copolymers based on cyclic carbonates)
     Polycarbonates, preparation
     Polycarbonates, preparation RL: IMF (Industrial manufacture); PRP (Properties); TEM (Technical or
     engineered material use); PREP (Preparation); USES (Uses)
        (polyester-; bioresorbable copolymers based on cyclic carbonates)
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97-93-8, uses 100-99-2, Triisobutylaluminum, uses 555-31-7, Aluminum isopropanolate 595-90-4, Tetraphenyltin 660-74-2 60004-29-7, Dioctyl
IT
    97-93-8. uses
     tin 129770-44-1
     RL: CAT (Catalyst use); USES (Uses)
        (bioresorbable copolymers based on cyclic carbonates)
     219811-64-0P
     RL: IMF (Industrial manufacture); PREP (Preparation)
        (bioresorbable copolymers based on cyclic carbonates)
                   230978-72-0P, 1,2-0-Isopropylidene-D-xylofuranose-3,5-
     224643-31-6P
     cyclic carbonate-L-trimethylenecarbonate copolymer 286382-68-1P,
     2,4-Dioxaspiro[5.5]undecane-8-ene-3-one-L-lactic acid copolymer
     286382-69-2P
     RL: IMF (Industrial manufacture); PRP (Properties); TEM (Technical or
     engineered material use); PREP (Preparation); USES (Uses)
        (bioresorbable copolymers based on cyclic carbonates)
     541-41-3, Ethyl chloroformate 20031-21-4, 1,2-0-Isopropylidene-D-
IT
     xylofuranose
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (bioresorbable copolymers based on cyclic carbonates)
     9004-10-8, Insulin, biological studies 127984-74-1, SOMATULINE
IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (bioresorbable copolymers based on cyclic carbonates)
             THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 23
RE
(1) Acemoglu; Macromolecules 1995, V28, P3030 HCAPLUS
(2) Anon; EP 0334062 A2 1989 HCAPLUS
(3) Barrera; Macromolecules 1995, V28, P425 HCAPLUS
(4) Berrera; US 5399665 1995 HCAPLUS
(5) Cai, J; Polymer International 1997, V42, P373
(6) Chiellini; Journal of Bioactive and Compatible Compatible Polymers 1994,
    V9, P153
(7) Dirk, W; Macromol Chem Phys 1994, V195, P1633
(8) Dirk, W; Macromol Chem Phys 1994, V195, P1649
(9) Elisseeff; Macromolecules 1997, V30(7) HCAPLUS
(10) Gerhart; US 5286763 1994 HCAPLUS
(11) Grijpma; Polymer 1993, V34(7) HCAPLUS
(12) Gruber; US 5359026 1994 HCAPLUS
(13) Gruber; US 5594095 1997 HCAPLUS
(14) Hrkach; US 5654381 1997 HCAPLUS
(15) John; Journal of Polymer Science, Part A: Polymer Chemistry 1997, V35,
    P1901 HCAPLUS
(16) Klee; Biomaterial-Tissue Interfaces, Advances in Biomaterials 1992, V10,
    P431 HCAPLUS
(17) Nyilas; US 4481353 1984 HCAPLUS
(18) Ouchi; Journal of Polymer Science, Part A: Polymer Chemistry 1997, V35,
    P377 HCAPLUS
(19) Schmidt; Macromolecules 1996, V29, P3674 HCAPLUS
(20) Shinoda; US 5747637 1998 HCAPLUS
(21) Sinclair; US 5502158 1996 HCAPLUS
(22) Tang; US 4916193 1990 HCAPLUS
(23) Tang; US 5066772 1991 HCAPLUS
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IT
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
        (bioresorbable copolymers based on cyclic carbonates)
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     L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
CN
     tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide,
     acetate (salt) (9CI) (CA INDEX NAME)
     CM
     CRN 108736-35-2
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CMF C54 H69 N11 O10 S2

Search done by Noble Jarrell

ANSWER 5 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

CM 2

CRN 64-19-7 CMF C2 H4 O2

L19

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2000:464011 HCAPLUS
AN
DN
     133:105344
ED
     Entered STN: 11 Jul 2000
     Preparation of technetium-99m labeled peptides for imaging
TI
     Dean, Richard T.; Buttram, Scott; Mcbride, William; Lister-James, John;
IN
     Civitello, Edgar R.
PA
     Diatide, Inc., USA
     U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 871,282.
so
     CODEN: USXXAM
DT
     Patent
LΑ
     English
IC
     ICM A61K051-00
     ICS A61M036-14
NCL
     424001690
     34-3 (Amino Acids, Peptides, and Proteins)
CC
     Section cross-reference(s): 8, 78
FAN.CNT 44
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                         KIND
                                DATE
                                             APPLICATION NO.
                                                                    DATE
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                          Α
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                                19991012
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         RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
PRAI US 1992-871282
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                          B2
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CLASS
                 CLASS PATENT FAMILY CLASSIFICATION CODES
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                        A61K051-00
 US 6086849
                 ICS
                        A61M036-14
                 NCL
                        424001690
                        A61K051/08; A61K051/08Z
 US 5965107
                 ECLA
     MARPAT 133:105344
os
     This invention relates to radiolabeled peptides and methods for producing
AB
     such peptides. Thus, peptide BAT-RALVDTLKFVTQAEGAKamide [BAT =
     HSCMe2CH2NHCH2CH2N (CH2CMe2SH) CH2CH2CH2CO] (P215) was prepared and
     radiolabeled with Tc-99m and used for localization and in vivo imaging of
     atherosclerotic plaque in the hypercholesterol rabbit model.
ST
     technetium labeled peptide prepn imaging
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·IT
     Imaging
        (preparation of technetium-99m labeled peptides for imaging)
TТ
     Peptides, preparation
     RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
        (preparation of technetium-99m labeled peptides for imaging)
     14133-76-7, Technetium-99, biological studies 32018-30-7 5153 RL: BSU (Biological study, unclassified); BIOL (Biological study)
                                                                    51532-41-3
TT
        (preparation of technetium-99m labeled peptides for imaging)
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     107-15-3, 1,2-Ethanediamine, reactions 824-94-2, 4-Methoxybenzyl
     chloride 954-81-4, n-(5-Bromopentyl)phthalimide
                                                          3695-77-0, Trityl
                4097-89-6, Tris(2-aminoethyl)amine
                                                       13206-46-7.
     mercaptan
     2-Bromo-2-methylpropanal 14660-52-7, Ethyl 5-bromovalerate
                                                                      55750-48-6,
     n-Methoxycarbonylmaleimide 57443-14-8 139262-23-0 153230-02-5
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (preparation of technetium-99m labeled peptides for imaging)
IT
     59880-97-6P 82989-21-7P 88650-17-3P 136721-52-3P 153229-93-7P
                    153229-95-9P 153229-96-0P
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     (Reactant or reagent)
        (preparation of technetium-99m labeled peptides for imaging)
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     BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent);
     USES (Uses)
        (preparation of technetium-99m labeled peptides for imaging)
TT
     152174-89-5DP, technetium-99m-labeled
                                              152174-90-8DP.
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     technetium-99m-labeled 152175-04-7DP, technetium-99m-labeled
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     study); PREP (Preparation); USES (Uses)
        (preparation of technetium-99m labeled peptides for imaging)
RE.CNT 57
              THERE ARE 57 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE
(1) Anon; WO 82301700 1982
(2) Anon; WO 85104958 1985
(3) Anon; EP 0174853 1986 HCAPLUS
(4) Anon; EP 0188256 1986 HCAPLUS
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(5) Anon; WO 86100360 1986

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(6) Anon; WO 86105920 1986
(7) Anon; WO 88102252 1988
(8) Anon; WO 8900051 1988 HCAPLUS
(9) Anon; WO 8902752 1988 HCAPLUS
(10) Anon; WO 8907456 1989 HCAPLUS
(11) Anon; WO 8910759 1989 HCAPLUS
(12) Anon; WO 8910760 1989 HCAPLUS
(13) Anon; WO 8912680 1989 HCAPLUS
(14) Anon; EP 0403243 1990 HCAPLUS
(15) Anon; WO 9010463 1990 HCAPLUS
(16) Anon; WO 9015818 1990 HCAPLUS
(17) Anon; WO 9015818 1990 HCAPLUS
(18) Anon; EP 90306428 1990
(19) Anon; WO 9101144 1990 HCAPLUS
(20) Anon; WO 9116919 1991 HCAPLUS
(21) Anon; WO 9117173 1991 HCAPLUS
(22) Anon; WO 9213572 1992 HCAPLUS
(23) Anon; WO 9321962 1993 HCAPLUS
(24) Anon; WO 9419024 1994 HCAPLUS
(25) Anon; WO 9533498 1995 HCAPLUS
(26) Baidoo; Bioconjugate Chem 1990, V1, P132 HCAPLUS
(27) Baidoo; Bioconjugate Chem 1990, V1, P132 HCAPLUS
(28) Bergstein; US 5279811 1994 HCAPLUS
(29) Bryson; InOrganic Chem 1990, V29, P2948 HCAPLUS
(30) Bryson; Inorg Chem 1988, V27, P2154 HCAPLUS (31) Bryson; Inorg Chem 1990, V29, P2948 HCAPLUS
(32) Byrne; US 4434151 1984 HCAPLUS
(33) Byrne; US 4571430 1986 HCAPLUS
(34) Byrne; US 4575556 1986 HCAPLUS
(35) Davison; US 4673562 1987 HCAPLUS
(36) Dean; US 5508020 1996 HCAPLUS
(37) Dean; US 5720934 1998 HCAPLUS
(38) Dean; US 5776428 1998 HCAPLUS
(39) Dean; US 5780007 1998 HCAPLUS
(40) Ege; US 4832940 1989 HCAPLUS
(41) Fritzberg; US 4444690 1984 HCAPLUS
(42) Fritzberg; US 4965392 1990 HCAPLUS
(43) Fritzberg; US 5175343 1992 HCAPLUS
(44) Fritzberg; US 5242679 1993 HCAPLUS
(45) Misra; Tet Let 1989, V30, P1885 HCAPLUS
(46) Misra; Tetrahedron Letters 1989, V30(15), P1885 HCAPLUS
(47) Neumeier; US 5302370 1994 HCAPLUS
(48) Nicolotti; US 4861869 1989 HCAPLUS
(49) Pearson; J Med Chem 1996, V39(7), P1372 HCAPLUS
(50) Pollak; US 5480970 1996 HCAPLUS
(51) Shocat; US 5061641 1991 HCAPLUS
(52) Srinivasan; US 4988496 1991 HCAPLUS
(53) Sundrehagen; Int J Appl Rad Isot 1983, V34, P1003 HCAPLUS
(54) Taylor; J Nucl Med 1990, V31, P885
(55) Troutner; US 4615876 1986 HCAPLUS
(56) Tubis; Int J Appl Rad Isot 1968, V19, P835 HCAPLUS
(57) Zubay; Biochemistry, Protein Structure and Function 1983, P3
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CN
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     alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-S-
     methyl-L-cysteinyl- (9CI) (CA INDEX NAME)
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Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-B

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Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-B

L19 ANSWER 6 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN AN 1999:780311 HCAPLUS

DN 132:20545

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ED
    Entered STN: 09 Dec 1999
     Technetium-99m labeled peptides for imaging
TI
    Dean, Richard T.; Buttram, Scott; Mcbride, William; Lister-James, John;
IN
     Civitello, Edgar R.
PA
    Diatide, Inc., USA
SO
    U.S., 23 pp., Cont.-in-part of U.S. Ser. No. 653,012, abandoned.
     CODEN: USXXAM
DT
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    Section cross-reference(s): 34, 63, 78
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os
AB
    This invention relates to radiolabeled peptides and methods for producing
     such peptides. Specifically, the invention relates to peptides, methods
     and kits for making such peptides, and methods for using such peptides to
     image sites in a mammalian body labeled with technetium-99m (Tc-99m) via a
     radiolabel-binding moiety covalently attached to a specific binding
     peptide via an amino acid side-chain of the peptide.
ST
    peptide technetium 99m imaging agent
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        (radiolabeled conjugates; technetium-99m labeled peptides for imaging)
IT
    Neoplasm
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      Imaging agents
      Infection
      Pancreas, neoplasm
      Radiopharmaceuticals
      Scintigraphy
      Test kits
      Thrombosis
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         (tumor; technetium-99m labeled peptides for imaging)
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                THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE.CNT 53
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```
Page 72
```

```
RE
(1) Albert; US 5686410 1997 HCAPLUS
(2) Anon; EP 82301700 1982
(3) Anon; EP 85104959 1985
(4) Anon; EP 174853 1986 HCAPLUS
(5) Anon; EP 188256 1986 HCAPLUS
(6) Anon; EP 86100360 1986
(7) Anon; EP 86105920 1986
(8) Anon; EP 88102252 1988
(9) Anon; WO 88900051 1989
(10) Anon; WO 8902752 1989 HCAPLUS
(11) Anon; WO 8907456 1989 HCAPLUS
(12) Anon; WO 8910759 1989 HCAPLUS
(13) Anon; WO 8910760 1989 HCAPLUS
(14) Anon; WO 8912625 1989 HCAPLUS
(15) Anon; WO 8912680 1989 HCAPLUS
(16) Anon; WO 8912680 1989 HCAPLUS
(17) Anon; EP 0403243 A1 1990 HCAPLUS
(18) Anon; EP 398143 1990 HCAPLUS
(19) Anon; EP 403243 1990 HCAPLUS
(20) Anon; WO 9010463 1990 HCAPLUS
(21) Anon; EP 90306428 1990
(22) Anon; EP 90402206 1991
(23) Anon; EP 9101144 1991
(24) Baidoo; Bioconjugate Chem 1990, V1, P132
(25) Bergstein; US 5279811 1994 HCAPLUS
(26) Bryson; Inorg Chem 1988, V27, P2154 HCAPLUS
(27) Bryson; Inorg Chem 1990, V29, P2948 HCAPLUS
(28) Byrne; US 4434151 1984 HCAPLUS
(29) Byrne; US 4571430 1986 HCAPLUS
(30) Byrne; US 4575556 1986 HCAPLUS
(31) Dean; US 5225180 1993 HCAPLUS
(32) Dean; US 5405597 1995 HCAPLUS
(33) Dean; US 5443815 1995 HCAPLUS
(34) Dean; US 5552525 1996 HCAPLUS
(35) Dean; US 5654272 1997 HCAPLUS
(36) Dean; US 5811394 1998 HCAPLUS
(37) Eg; US 4673562 1987 HCAPLUS
(38) Ege; US 4832940 1989 HCAPLUS
(39) Fritzberg; US 4444690 1984 HCAPLUS
(40) Fritzberg; US 4965392 1990 HCAPLUS
(41) Gansow; US 4472509 1984 HCAPLUS
(42) Lister-James; The Journal of Nuclear Medicine 1994, V35(5), P257P
(43) Lyle; US 5382654 1995 HCAPLUS
(44) Misra; Tet Lett 1989, V30, P1885 HCAPLUS
(45) Morgan; US 4986979 1991 HCAPLUS
(46) Nicolotti; US 4861869 1989 HCAPLUS
(47) Shochat; US 5061641 1991 HCAPLUS
(48) Srinivasan; US 4988496 1991 HCAPLUS
(49) Sundrehagen; Int J Appl Rad Isot 1983, V34, P1003 HCAPLUS
(50) Taylor; J Nucl Med 1990, V31, P885
(51) Troutner; US 4615876 1986 HCAPLUS
(52) Tubis; Int J Appl Rad Isot 1968, V19, P835 HCAPLUS
(53) Zubay, G; Biochemistry Protein Structure and Function 1983, P3
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Absolute stereochemistry.

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RN

189688-27-5 HCAPLUS
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naphthalenyl)-D-alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-S-methyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-B

L19 ANSWER 7 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

AN 1999:732950 HCAPLUS

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                         C07K014/52; C07K014/655; C07K014/78
     The invention relates to radiotherapy with somatostatin-derived peptides labeled with medically useful metal ions. The invention in particular
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provides for methods and reagents for labeling somatostatin-derived peptides with perrhenate, in which a solution including somatostatin-derived peptide analog containing at least one disulfide bond is provided, the solution is reacted with stannous ions and with a radioisotope, wherein the stannous ions are sufficient to substantially reduce the disulfide bonds of the peptide and the radioisotope, and the radiolabeled somatostatin-derived peptide analog recovered. Also provided are methods for regional administration of radiolabeled somatostatin-derived peptides, methods for enhanced regional retention of radiolabeled somatostatin-derived peptides, methods for treatment of arthritis using radiolabeled somatostatin derived peptides, and methods for stabilizing radiolabeled somatostatin derived peptides. somatostatin peptide radiolabeled prepn rheumatoid arthritis; radiotherapy rheumatoid arthritis radiolabeled somatostatin peptide; tumor radiotherapy rhenium labeled somatostatin peptide Proteins, general, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (blood; effect of carrier mols. on biodistribution of rhenium-labeled somatostatin-derived peptide) Colloids (drug delivery systems; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Neuroglia (glioblastoma multiforme; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Drug delivery systems (microparticles; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Pleura Prostate gland (neoplasm; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Antitumor agents Pancreas, neoplasm Pharmacokinetics Radiotherapy Rheumatoid arthritis Test kits (radiotherapy with somatostatin-derived peptides labeled with 188Re or Somatostatin receptors RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Albumins, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (serum; effect of carrier mols. on biodistribution of rhenium-labeled somatostatin-derived peptide) Lung, neoplasm (small-cell carcinoma; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) Globulins, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (.gamma.-; effect of carrier mols. on biodistribution of rhenium-labeled somatostatin-derived peptide) 10043-66-0D, Iodine 131, somatostatin derived peptides labeled with, biological studies RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (biodistribution of radiolabeled somatostatin analogs) 14378-26-8DP, Rhenium 188, somatostatin derived peptides labeled with, biological studies 103222-11-3DP, RC-160, radiolabeled RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses) (radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) 14133-76-7DP, Technetium 99, somatostatin derived peptides labeled with, biological studies 14998-63-1DP, Rhenium 186, somatostatin derived peptides labeled with, biological studies 51110-01-1DP, Somatostatin 51110-01-1DP, Somatostatin,

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Audet 09/870087 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (radiotherapy with somatostatin-derived peptides labeled with 188Re or 131167-89-0D, radiolabeled RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) 108736-35-2DP, radiolabeled RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) 815-85-0, Stannous tartrate, reactions 22541-90-8, Stannous ion, reactions 87552-16-7, 186Re-Perrhenate 122123-28-8, 188Re-Perrhenate RL: RCT (Reactant); RACT (Reactant or reagent) (radiotherapy with somatostatin-derived peptides labeled with 188Re or 50-81-7, L-Ascorbic acid, uses RL: MOA (Modifier or additive use); USES (Uses) (stabilizer; radiotherapy with somatostatin-derived peptides labeled with 188Re or 186Re) RE.CNT 91 THERE ARE 91 CITED REFERENCES AVAILABLE FOR THIS RECORD (1) Akers, M; J of Paren Sci & Tech 1982, V36, P222 HCAPLUS (2) Anderson; US 5169933 1992 HCAPLUS (3) Anon; EP 0196669 1986 HCAPLUS (4) Anon; EP 0237150 A2 1987 HCAPLUS (5) Anon; EP 0250013 1987 HCAPLUS (6) Anon; EP 0284071 A2 1988 HCAPLUS (7) Anon; WO 9015818 1989 HCAPLUS (8) Anon; CA 2016235 1990 HCAPLUS (9) Anon; GB 2225579 A 1990 HCAPLUS (10) Anon; EP 89114365 1990 (11) Anon; WO 9213572 1992 HCAPLUS (12) Anon; EP 92810381 1992 (13) Anon; US 9306029 1994 (14) Anon; EP 94810008 1994 (15) Anon; WO 9511045 1994 HCAPLUS (16) Anon; US 9406274 1995 (17) Anon; US 9408335 1995 (19) Bard, D; Ann NY Acad Sci 1993, V680, P451 HCAPLUS (20) Bard, D; Br J Cancer 1990, V62, P919 HCAPLUS (21) Bender, H; J NucL Med Abstract Book 1995, V5, P183P(22) Bender, H; Radionuclides for Receptors (published after filing date of

Page 77

IT

IT

IT

RE

- (18) Ballinger, J; Eur J Nuc Med 1981, V6, P153 HCAPLUS

- parent application) 1995
- (23) Bernardi; US 5225530 1993 HCAPLUS
- (24) Cai, R; Proc Natl Acad Sci USA 1986, V83, P1896 HCAPLUS
- (25) Chinol, M; J Nuc Med 1993, V34, P1536 HCAPLUS
- (26) Cox, P; 7th Int'l Sumpos on Radiopharm 1991, P16
- (27) Coy; US 4904642 1990 HCAPLUS
- (28) Crockford; US 4424200 1984 HCAPLUS
- (29) Dean; US 5162505 1992 HCAPLUS
- (30) Dean; US 5225180 1993 HCAPLUS
- (31) Dean; US 5405597 1995 HCAPLUS
- (32) Dean; US 5443815 1995 HCAPLUS
- (33) Deutsch; US 5384113 1995 HCAPLUS
- (34) Deutsch, E; Eur J Nuc Med 1993, V20, P1113 MEDLINE
- (35) Dox; The Harper Collins Illustrated Medical Dictionary 1993, P310 (36) Fioravanti, A; La Clin Ter (English abstract provided) 1993, V142, P453 MEDLINE
- (37) Fischman, A; J Nucl Med 1993, V34(12), P2253 HCAPLUS
- (38) Flanagan; US 5632969 1997 HCAPLUS
- (39) Fritzberg; US 5091514 1992 HCAPLUS
- (40) Griffiths; US 5128119 1992 HCAPLUS
- (41) Hansen; US 5328679 1994 HCAPLUS
- (42) Hnatowich; US 4479930 1984 HCAPLUS
- (43) Hnatowich; US 4668503 1987 HCAPLUS
- (44) Hoefnagel, C; Anticancer Drugs 1991, V2, P107 HCAPLUS
- (45) Hosono, M; J Nucl Med Abstract Book 1995, V5, P72P
- (46) Hynes, R; Cell 1992, V69, P11 HCAPLUS

```
Audet 09/870087
(47) Ill, C; J Cell Bio 1984, V99, P2140 HCAPLUS
(48) Khaw, B; J Nucl Med 1982, V23(11), P1011 MEDLINE
(49) Knight, L; J Nucl Med 1990, V31(5, 209)
(50) Kondo, M; Peptide: Chemistry and Biology 1992, P425 HCAPLUS
(51) Kraus, J; Bilchem and Biophy Res Comm 1984, V124(3), P939 HCAPLUS
(52) Krenning, E; Eur J Nucl Med 1993, V20, P716 MEDLINE
(53) Lyle; US 5382654 1995 HCAPLUS
(54) Matucci-Cerinic, M; Drugs Exp Clin Res 1992, V18, P53 MEDLINE
(55) McBride; US 5620675 1997 HCAPLUS
(56) Morgan; US 4986979 1991 HCAPLUS
(57) Morgan; US 5376356 1994 HCAPLUS
(58) Oberg, K; Cancer Treat Rev 1994, V20, P331 MEDLINE
(59) Olexa; US 4427646 1984 HCAPLUS
(60) Pimm, M; Int'l J Pharm 1992, V79, P77 HCAPLUS
(61) Pinski, J; Br J Cancer 1994, V70, P886 HCAPLUS
(62) Pinski, J; Cancer Res 1994, V54, P5895 HCAPLUS
(63) Pipes; US 5021235 1991 HCAPLUS
(64) Rajagopolan; US 5371184 1994 HCAPLUS
(65) Rhodes; US 5078985 1992 HCAPLUS
(66) Rhodes; US 5102990 1992 HCAPLUS
(67) Rhodes; US 5460785 1995 HCAPLUS
(68) Riva, P; J Nuc Med 1994, V5, P144P
(69) Riva, P; J Nucl Med Abstract Book 1995, V5, P213P
(70) Saiki; US 5236903 1993 HCAPLUS
(71) Schasteen; US 5039662 1991 HCAPLUS
(72) Shochat; US 5051641 1991
(73) Sonnenberg, A; Exp Cell Res 1991, V197, P234 HCAPLUS
(74) Swanson, D; J Nucl Med 1993, V34(231P Abstract)
(75) Szabo; US 4612302 1986 HCAPLUS
(76) Tam; US 5229490 1993 HCAPLUS
(77) Tandon, N; Riochem J 1991, V2724, P535 (78) Thakur; US 5011676 1991
(79) Thakur; US 5308603 1994
(80) Tofe, A; J of Nuc Med 1976, V17, P820 HCAPLUS
(81) Tofe, A; J of Nuc Med 1979, V21, P366
(82) Tolman; US 4732864 1988 HCAPLUS
(83) Vanderheyden; US 5679318 1997 HCAPLUS
(84) Will, R; Ann Rheum Dis 1993, V51, P262
(85) Wraight, E; Brit J Rad 1992, V65, P112 MEDLINE
(86) Yamada; US 5092885 1992 HCAPLUS
(87) Yamada, K; J Biol Chem 1992, V266(20), P12809
(88) Zamora; US 5443816 1995 HCAPLUS
(89) Zamora, P; Int J Cancer 1996, V65, P214 HCAPLUS
(90) Zamora, P; J Nucl Med Abstract Book 1995, V5, P42P
(91) Zamura; Applied Radiation and Isotopes 1995
```

BIOL (Biological study); PREP (Preparation); USES (Uses)

RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use);

(radiotherapy with somatostatin-derived peptides labeled with 188Re or

108736-35-2DP, radiolabeled

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L19 ANSWER 8 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
     1997:276721 HCAPLUS
AN
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     126:343883
ED
     Entered STN: 30 Apr 1997
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     Preparation and antitumor activity of radioactive peptide complexes
     McBride, William; Dean, Richard T.
IN
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                        A61K038-00; A61K051-00
                 NCL
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                        A61K051/08; A61K051/08Z; C07K014/655A
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     MARPAT 126:343883
     This invention relates to therapeutic reagents and peptides,
     radiodiagnostic reagents and peptides, and methods for producing label radiodiagnostic agents. Specifically, the invention relates to linear
     peptide derivs. and analogs of somatostatin, and embodiments of such
     peptides radiolabeled with a radioisotope, as well as methods and kits for
     making, radiolabeling and using such peptides for radiodiagnostic and
     radiotherapeutic purposes. The invention specifically relates to linear
     peptide derivs. and analogs of somatostatin radiolabeled with
     technetium-99m and uses thereof as scintigraphic imaging agents. The
     invention so specifically relates to liner peptide derivs. and analogs of somatostatin radiolabeled with cytotoxic radioisotopes such as rhenium-186
     and rhenium-188 for use as radiotherapeutic agents. Methods and kits for
     making, radiolabeling and using such peptides diagnostically and
     therapeutically in a mammalian body are also provided.
     antitumor agent radioactive peptide complex prepn; technetium peptide
ST
     complex prepn antitumor agent; rhenium peptide complex prepn antitumor
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agent
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
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     BIOL (Biological study); PREP (Preparation); USES (Uses)
        (complexes, technetium-99m and radioactive rhenium complexes; preparation
        and antitumor activity of radioactive peptide complexes)
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         (preparation and antitumor activity of radioactive peptide complexes)
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     technetium-99m complexes 189688-30-0DP, technetium-99m complexes
     RL: SPN (Synthetic preparation); PREP (Preparation)
         (preparation and antitumor activity of radioactive peptide complexes)
TΤ
     161888-99-9DP, technetium-99m complexes 189688-26-4DP,
     technetium-99m complexes
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     study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
         (preparation and antitumor activity of radioactive peptide complexes)
     161888-99-9 HCAPLUS
RN
     L-Threonine, 1,1'-[[(carboxymethyl)imino]di-2,1-ethanediyl]bis[N-
CN
     (carboxymethyl)glycyl-3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
     tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)
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Absolute stereochemistry.

PAGE 1-A

## PAGE 1-B

PAGE 1-C

PAGE 2-A

PAGE 2-B

RN

L-Threoninamide, N6-[5-[(2-mercapto-2-methylpropyl)][2-[(2-mercapto-2-methylpropyl)] amino]ethyl]amino]-1-oxopentyl]-L-lysyl-3-(2-naphthalenyl)-D-alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-S-methyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

189688-26-4 HCAPLUS

PAGE 1-A

PAGE 1-B

PAGE 2-B

IT 161888-99-9P 161889-27-6P 189688-26-4P
 189688-27-5P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)

Search done by Noble Jarrell

(preparation and antitumor activity of radioactive peptide complexes)
RN 161888-99-9 HCAPLUS
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Absolute stereochemistry.

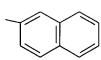
PAGE 1-A

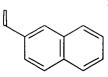
PAGE 1-B

PAGE 1-C

PAGE 2-A

PAGE 2-B





RN 161889-27-6 HCAPLUS

CN L-Threoninamide, N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl-3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-A

PAGE 2-B

СО2Н СО2Н

RN 189688-26-4 HCAPLUS

CN L-Threoninamide, N6-[5-[(2-mercapto-2-methylpropyl)][2-[(2-mercapto-2-methylpropyl)] amino]ethyl]amino]-1-oxopentyl]-L-lysyl-3-(2-naphthalenyl)-D-alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-S-methyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-B

189688-27-5 HCAPLUS

RN

CN

L-Threoninamide, N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl-N6-[5-[(2-mercapto-2-methylpropyl)[2-[(2-mercapto-2-methylpropyl)amino]ethyl]amino]-1-oxopentyl]-L-lysyl-3-(2-naphthalenyl)-D-alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-

L-valyl-S-methyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-B

IT 161889-27-6DP, technetium-99m complexes 189688-27-5DP, technetium-99m complexes
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation and antitumor activity of radioactive peptide complexes)

RN 161889-27-6 HCAPLUS

L-Threoninamide, N-[2-[[2-[bis(carboxymethyl)amino]ethyl](carboxymethyl)amino]ethyl]-N-(carboxymethyl)glycyl-3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A

PAGE 1-B

PAGE 2-A

PAGE 2-B

189688-27-5 HCAPLUS
L-Threoninamide, N-[2-[[2-[bis(carboxymethy1)amino]ethy1](carboxymethy1)amino]ethy1]-N-(carboxymethy1)glycy1-N6-[5-[(2-mercapto-2-methy1propy1)[2-CN

[(2-mercapto-2-methylpropyl)amino]ethyl]amino]-1-oxopentyl]-L-lysyl-3-(2-naphthalenyl)-D-alanyl-S-methyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-S-methyl-L-cysteinyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

## PAGE 1-B

L19 ANSWER 9 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN AN 1996:701926 HCAPLUS

Audet 09/870087

Page 91

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DN
     125:339095
ED
     Entered STN: 27 Nov 1996
     Preparation of microballs containing active agent and biocompatible
TI
     polymer
IN
     Ruiz, Jean-Marc
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     Societe de Conseils de Recherches et d'Applications Scientifiques (SCRAS),
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           8 pp., Cont.-in-part of U.S. Ser. No. 67, 354, abandoned.
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NCL
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 US 5569467
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     An active ingredient, a biocompatible polymer, and a supporting phase, such as silicone oil, are stirred at a temperature above the glass transition
     temperature of the polymer and below the temperature at which any of the ingredients
     vaporizes or degrades. Stirring is continued until microballs of the
     desired diameter are formed, whereafter the mixture is cooled and the
     microballs are separated from the supporting phase. The microballs are
     substantially spherical, substantially smooth on their external surface,
     and have substantially no active ingredient on their external surface;
     thus no burst effect (rapid release phase) occurs when the particles are
     first administered in a sustained-release preparation. The process requires no
     solvent or mech. treatment of the active ingredient. Thus, 5 g
     lactide/glycolide (50:50) copolymer particles were dispersed in 500 mL
     silicone oil at 100-120.degree., and 0.980 g somatuline pamoate was added while stirring. After stirring for 30 min, the mixture was heated to
     130.degree., stirring was stopped, and the mixture was cooled to 25.degree..
     The stirring-induced shear formed particles with average diameter 5-10 .mu.m.
ST
     drug microparticle biodegradable polymer; microsphere drug lactide
     glycolide copolymer
TT
     Biodegradable materials
         (polymers; preparation of microballs containing active agent and biocompatible
        polymer)
IT
     Shear
        (preparation of microballs containing active agent and biocompatible polymer)
IT
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     RL: BAC (Biological activity or effector, except adverse); BSU (Biological
     study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
     (Uses)
        (preparation of microballs containing active agent and biocompatible polymer)
TT
     Polymers, biological studies
     RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
         (preparation of microballs containing active agent and biocompatible polymer)
IT
     Gels
        (supporting phase; preparation of microballs containing active agent and
        biocompatible polymer)
     Castor oil
     Oils
     Peanut oil
     Siloxanes and Silicones, uses
     RL: NUU (Other use, unclassified); USES (Uses)
        (supporting phase; preparation of microballs containing active agent and biocompatible polymer)
TT
     Spheres
         (micro-, preparation of microballs containing active agent and biocompatible
        polymer)
IT
     Pharmaceutical dosage forms
         (microspheres, preparation of microballs containing active agent and
        biocompatible polymer)
     Fats and Glyceridic oils
IT
     RL: NUU (Other use, unclassified); USES (Uses)
         (sesame, supporting phase; preparation of microballs containing active agent and
        biocompatible polymer)
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(preparation of microballs containing active agent and biocompatible polymer) 24980-41-4, Poly-.epsilon.-caprolactone 25248-42-4, Poly[oxy(1-oxo-1,6-TΤ 26780-50-7, Lactide/glycolide copolymer hexanediyl)] 34346-01-5. Lactic acid/glycolic acid copolymer

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of microballs containing active agent and biocompatible polymer) 637-12-7D, Aluminum stearate, mixture with sesame oil 9003-39-8, PVP IT RL: NUU (Other use, unclassified); USES (Uses)

(supporting phase; preparation of microballs containing active agent and biocompatible polymer)

IT 183736-93-8

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(preparation of microballs containing active agent and biocompatible polymer)

RN 183736-93-8 HCAPLUS

L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-Dtryptophyl-L-lysyl-L-valyl-L-cysteinyl-, 8-[hydrogen 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylate]], cyclic (2.fwdarw.7)-disulfide, acetate (salt) (9CI) (CA INDEX NAME)

CM

CN

CRN 183736-92-7 CMF C77 H83 N11 O15 S2

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PAGE 1-B

CM 2

CRN 64-19-7 CMF C2 H4 O2

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DN
    123:208880
    Entered STN: 15 Sep 1995
ED
ΤI
    Process for preparing a controlled-release pharmaceutical composition of
    peptides
IN
    Orsolini, Piero; Heimgartner, Frederic
    Debio Recherche Pharmaceutique S.A., Switz.
PA
so
    U.S., 6 pp. Cont.-in-part of U.S. 5,134,122.
    CODEN: USXXAM
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L19 ANSWER 10 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN

DT Patent

LA English

IC ICM A61K009-14

ICS A61K037-24; A61K009-48

NCL 424489000

CC 63-6 (Pharmaceutic FAN.CNT 3	cals)		•
PATENT NO.	KIND DATE	APPLICATION NO.	DATE
PI US 5439688	A 19950808	US 1991-790033	19911112 <
US 5134122	A 19920728	US 1990-555973	19900720 <
CH 681425	A 19930331	CH 1990-3616	19901114 <
US 5225205	A 19930706	US 1992-836478	19920218 <
PRAI US 1990-555973	A2 19900720	<	
CH 1990-3616	A 19901114	<	
CH 1989-2829	A 19890728	<	
CLASS			
PATENT NO. CLASS	PATENT FAMILY CLA	SSIFICATION CODES	
US 5439688 ICM	A61K009-14		
ICS	A61K037-24; A61K0	09-48	
NCL	424489000		

AB A pharmaceutical composition is prepared in the form of microparticles or of an implant comprising a biodegradable polymer selected from poly-1,4-butylene succinate, poly-2,3-butylene succinate, poly-1,4-butylene fumarate, and poly-2,3-butylene fumarate and incorporating as the active substance the pamoate, tannate, stearate or palmitate of a natural or of a synthetic peptide comprising 3-45 amino acids, such as LH-RH, somatostatin, GH-RH, calcitonin, or one of their synthetic analogs or homologs. The process comprises dry-blending the ingredients in the form of powders, pre-compressing and preheating the mixture and then extruding the pre-compressed and pre-heated mixture The product resulting from the extrusion step can then be comminuted and finally sieved. A powder mixture containing poly-1,4-butylene succinate and D-Trp6-LH-RH pamoate was heated to 90.degree. and extruded to give filaments, which were milled and sieved to obtain particles with an average diam of <180 .mu.m. The in vivo tests for

determination of blood testosterone levels in rats confirmed that the release of the active substance remained sustained for .gtoreq.25 days.

ST peptide salt polyester controlled release implant; microparticle LHRH

pamoate polybutylene succinate

IT Polyesters, biological studies

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (controlled-release peptide formulations containing biodegradable polyesters)

IT Pharmaceutical dosage forms

(implants, controlled-release peptide formulations containing biodegradable polyesters)

IT Pharmaceutical dosage forms

(microparticles, controlled-release peptide formulations containing biodegradable polyesters)

IT 9007-12-9D, Calcitonin, salts 9034-39-3D, Growth hormone-releasing hormone, salts 9034-40-6D, LH-RH, salts 26247-20-1, Poly-1,4-butylene succinate 36813-67-9 45127-28-4 51110-01-1D, Somatostatin, salts 78969-57-0D, alkyl derivs., pamoates 103527-38-4 111755-78-3D, alkyl derivs., pamoates 124409-34-3 124508-66-3 145020-14-0 145020-15-1 145020-16-2 145107-38-6 145256-99-1 145699-79-2 168022-60-4

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (controlled-release peptide formulations containing biodegradable polyesters)

IT 145020-16-2

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(controlled-release peptide formulations containing biodegradable polyesters)

RN 145020-16-2 HCAPLUS

CN L-Threoninamide, D-phenylalanyl-L-cysteinyl-L-tyrosyl-D-tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide, 4,4'-methylenebis[3-hydroxy-2-naphthalenecarboxylate] (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 99660-13-6 CMF C50 H67 N11 O10 S2

CM 2

CRN 130-85-8 CMF C23 H16 O6

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L19 ANSWER 11 OF 11 HCAPLUS COPYRIGHT 2004 ACS on STN
     1991:608611 HCAPLUS
DN
     115:208611
     Entered STN: 15 Nov 1991
ED
     Preparation of serine-containing decapeptides as LH-RH antagonists
TΙ
IN
     Coy, David H.; Moreau, Jacques Pierre
PA
     Tulane Educational Fund, Inc., USA
     U.S., 16 pp. Cont.-in-part of U.S. Ser. No. 352,140, abandoned.
SO
     CODEN: USXXAM
DT
     Patent
LΑ
     English
IC
     ICM A61K037-02
     ICS A61K009-48; A61K009-20; C07K007-06
NCL
     530328000
     34-3 (Amino Acids, Peptides, and Proteins)
     Section cross-reference(s): 1
FAN.CNT 3
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     US 5003011
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                                  19910326
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                                               US 1987-65765
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     US 5073624
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                                  19911002
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                                               NO 1991-2254
                                                                       19910612 <--
                           Α
                                  19910812
PRAI US 1985-721330
                                  19850409
     US 1985-798239
                                  19851114
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     US 1986-879338
                                  19860627
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     US 1987-65765
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     US 1989-352140
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     US 1989-421245
                                  19891013
                                             <--
     WO 1990-US5842
                                  19901011
CLASS
 PATENT NO.
                  CLASS PATENT FAMILY CLASSIFICATION CODES
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                  ICM
                         A61K037-02
                         A61K009-48; A61K009-20; C07K007-06
                  ICS
                  NCL
                         530328000
os
     MARPAT 115:208611
     Title compds. Ac-Z1-Z2-Z3-Ser-Z5-Z6-Z7-Z8-Z9-Z10 [Z1-Z3 =
     D-.beta.-naphthylalanine (Nal), D-p-X-Phe; Z5 = p-X-Phe; Z6 = D-Lys,
     D-Arg, .beta.-Nal, D-.beta.-Nal, D-Trp, D-p-X-Phe, D-Lys(R); Z7 =
     p-X1-Phe, cyclohexylalanine, Trp; Z8 = Arg, Lys, Lys(R); Z9 = Pro; Z10 = D-Ala-NH2, Gly-NH2, D-Ser, D-Ser-NH2; X = halo, H, NH2, NO2, OH, C1-3
     alkyl; X1 = X, C2F5; R = H, C1-10 (cyclo)alkyl, aryl; with provisos], which are LH-RH antagonists useful in the treatment of hormone-dependent
     cancers of the breast, prostate, and ovary, were prepared Thus
     Ac-D-.beta.-Nal-D-Phe-D-Phe-Ser-Tyr-D-Arg-Phe-Arg-Pro-D-Ala-NH2 (I) was
     synthesized using a Beckman 990B peptide synthesizer starting from
     benzhydrylamine-polystyrene resin and Boc-D-Ala-OH, Boc-Pro-OH,
     Boc-Arg(Tos)-OH, Boc-Phe-OH, Boc-D-Arg(Tos)-OH, Boc-Tyr-OH,
     Boc-Ser(Bz1)-OH, Boc-D-Phe-OH, and Boc-D-.beta.-Nal-OH. The resin-bound
     peptide was deprotected at the N-terminal end, acetylated, and treated
     with a HF solution containing anisole and dithiothreitol to give I. I injected
     s.c. at 15 .mu.g/day (for 6 days) into female mice implanted with human
     MCF-7 mammary tumor decreased the size of the tumor to 34% of the control
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Audet 09/870087

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tumor.
ST
     seryl decapeptide prepn LHRH antagonist; neoplasm inhibitor seryl
     decapeptide
     Neoplasm inhibitors
IT
         (serine-containing decapeptides)
IT
     3978-80-1
                 7764-95-6
                             13139-15-6
                                             13734-34-4
                                                           13836-37-8
     18942-49-9
                  23680-31-1
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     RL: RCT (Reactant); RACT (Reactant or reagent)
         (peptide coupling of, in preparation of LH-RH antagonists)
     136830-00-7DP, benzhydrylamine resin-bound
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     (Reactant or reagent)
        (preparation and reaction of, in preparation of LH-RH antagonists)
ΙT
     5241-64-5P
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        (preparation of)
IT
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                    57773-63-4P
                                  96394-82-0P
                                                  106881-54-3P
                                                                  106881-55-4P
     108736-35-2P
                     110014-26-1P
                                     110014-29-4P
                                                      110014-30-7P
                     110014-36-3P
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     110014-34-1P
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     136829-99-7P
     RL: SPN (Synthetic preparation); PREP (Preparation)
     (preparation of, as LH-RH antagonist) 9034-40-6DP, LH-RH, analogs
IT
     RL: SPN (Synthetic preparation); PREP (Preparation) (preparation of, as LH-RH antagonists)
     67-64-1, Acetone, reactions
     RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in preparation of LH-RH antagonists)
ΙT
     136830-01-8D, benzhydrylamine resin-bound
     RL: RCT (Reactant); RACT (Reactant or reagent)
        (resin cleavage of, in preparation of LH-RH antagonists)
IT
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        (preparation of, as LH-RH antagonist)
RN
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     L-Threoninamide, 3-(2-naphthalenyl)-D-alanyl-L-cysteinyl-L-tyrosyl-D-
CN
     tryptophyl-L-lysyl-L-valyl-L-cysteinyl-, cyclic (2.fwdarw.7)-disulfide
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(9CI) (CA INDEX NAME)

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